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# *The American Heart Journal*

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# The American Heart Journal

VOL. VI FEBRUARY, 1931 No. 3


## Original Communications

# INSTRUMENTAL METHODS IN THE STUDY OF PERIPHERAL VASCULAR DISEASE*†


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### INTRODUCTION

THE study of peripheral vascular disease lends itself to instrumental measurement and tends to become a more exact science. With the desire in modern medicine for mathematical precision, it is essential to recognize the limitations and fallacies of the methods applied, as well as their advantages. Unrecognized physiological variations may nullify what appear to be valuable pathological data.

The major part of this investigation deals with organic, occlusive arterial disease (chiefly thrombo-angiitis obliterans) and the effects of sympathetic ganglionectomy. The importance of clinical history and examination and the well-recognized postural tests cannot be overemphasized. Nevertheless, much scope is still left for more exact methods of elucidating the state of disease and the results of certain procedures. The two most important instrumental methods of studying peripheral vascular disease are the measurement of surface temperature and oscillometry. Brown has stressed the value of the former method, and its comparative value is examined in this paper in relation to oscillometric measurement. The advantages and disadvantages of digital examination are considered, as are also the relative merits of the Tycos and Pachon oscillometers. Both instruments are made on similar aneroid principles, and record the amplitude of pulsations in arbitrary units. In the data given in this paper the Tycos measurements are expressed in millimeters and the Pachon, in half-units. The former instrument furnishes a permanent record, but in the use of the latter, the measurement must be noted at the time of examination and expressed numerically by the observer. In digital examination the

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femoral, popliteal, posterior tibial, and dorsalis pedis arteries are palpated. It will be seen later that the different methods employed change their relative values when applied to different aspects of the problem and that they must therefore be considered under several headings. Although this work was commenced as a purely technical study with the advice and help of internists and neurologic surgeons of The Mayo Clinic, it has been found possible to observe and analyze several interesting and fundamental phenomena of physiological and pathological significance.

After some experience the digital palpation of superficial arteries offers no special difficulty. Occasionally pulsation in the warm fingers of an observer may simulate pulsation in the patient. The pulsation of a posterior tibial artery may not be obvious in a cold room and yet may be quite easily made out in a warm one. Palpation of an artery in a case of thrombo-angiitis obliterans by a previous observer may produce a temporary spasm which leads to an erroneous impression.

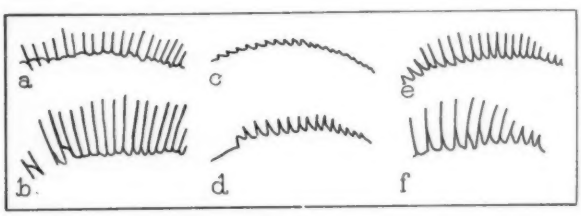


Fig. 1.—*a, b,* Variation in record of pulsations at the calf obtained by moving bag laterally; *c, d, e, f,* variation in pulsations at the ankle in different normal persons.

Even apart from these more obvious factors, it is not impossible for trained observers to differ, and to feel the need for the confirmation of digital impressions.

In using any form of oscillometer it is advisable to mark the exact site of measurement. The following sites may be taken: (1) femoral triangle; (2) immediately above patella; (3) immediately below patella; (4) 5 cm. below patella; (5) 10 cm. below patella; (6) 15 cm. below patella; (7) just above ankle, and (8) foot. In many cases measurements above the knee can be omitted. They tend to be less constant in view of the bulky musculature, and it is difficult to reapply the bag at the same site as before. Below the knee, a constant position in the horizontal axis or circumference of the limb is more easily attained. This can be done by placing the rubber valve connections along the anterior border of the tibia. There are two sites where false readings may be registered: (1) just below the patella, owing to the irregular contour produced by tendinous insertions, and (2) at the calf, owing to the large musculature. The latter is particularly well shown in Fig. 1 *a* and *b*. Both tracings were made 10 cm. below the patella, and the increased amplitude of the tracing shown in Fig. 1 *b*

was produced by shifting the pneumatic bag slightly to the outer side. This is the preferable point of application at this particular site. The readings at the lower border of the patella often appear to be reduced both in blood pressure and amplitude of pulsation and are thus somewhat anomalous. Five centimeters below the patella and just above the ankle joint are convenient sites in the leg to be used as a routine.

For the measurement of pulsation in the foot, palm, and fingers, it is advisable to use special pneumatic bags which can be connected to the Tycos apparatus. The blood pressure recorded by the narrower pneumatic bag is, for mechanical reasons, considerably higher than that obtained with the larger bag usually employed, and therefore is not recorded in the tables. For similar reasons the amplitude of pulsation at the same site would be relatively higher with the smaller bag, but this is not obvious, owing to the smaller caliber of the vessels in the distal regions mentioned. These measurements made at the more peripheral points of the limbs will be seen later to be of very great significance.

TABLE I

OSCILLOMETRIC AND SPHYGMOMANOMETRIC VALUES FOR A NORMAL ADULT*

| SITE | | TYCOS APPARATUS | | | PACHON APPARATUS | | |
|---|---|---|---|---|---|---|---|
| | | BLOOD PRESSURE | | | BLOOD PRESSURE | | |
| | DIGITAL PALPATION, GRADE | SYSTOLIC | DIASTOLIC | OSCILLOMETRIC UNITS | SYSTOLIC | DIASTOLIC | OSCILLOMETRIC UNITS |
| Femoral region | 4 | 170 | 100 | 26 | 200 | 120 | 20 |
| Above knee | | 140 | 90 | 22 | 170 | 100 | 16 |
| Popliteal region | 4 | | | | | | |
| Below patella | | 120 | 75 | 14 | 140 | 80 | 8 |
| 5 cm. below patella | | 125 | 80 | 20 | 150 | 80 | 15 |
| 10 cm. below patella | | 125 | 80 | 16 | 140 | 80 | 14 |
| 15 cm. below patella | | 125 | 80 | 12 | 150 | 80 | 10 |
| Ankle | | 122 | 80 | 8 | 150 | 80 | 8 |
| Posterior tibial region | 4 | | | | | | |
| Dorsalis pedis region | 4 | | | | | | |
| Foot | | | | 3 | | | |
| Brachial region | | 125 | 80 | 12 | 130 | 80 | 8 |

*Oscillometric values are given in the arbitrary units that are explained in the text. The grades used to designate the results of digital palpation are recorded in a scale of 4 to 0, in which 4 indicates maximal pulsation and 0, none. Blood pressure is given in millimeters of mercury.

In Table I are recorded a series of values for a normal adult. It will be seen that the oscillometric values correspond as far as relative values are concerned. The blood pressures registered by the Pachon apparatus tend to be higher than the real values. This is a purely mechanical factor and is of no particular significance when once recognized.

Although the values in Table I are supposed to be normal it would be more correct to admit that it is almost impossible to define normal

or average values. In Fig. 1, tracings *d*, *e* and *f* represent readings at the ankle in three separate adults about thirty years old, with no vascular abnormality. Tracings *e* and *f* were those of normal physicians and tracing *d* that of a patient with chronic gastric ulcer. The marked differences in the three are obvious. In the same figure, tracings *c* and *d* represent readings at the same site and of the same patient, but taken a few minutes apart. This rapid variation is unusual, and the small initial amplitude may possibly be due to emotional vasoconstrictor impulses. It is a potential fallacy that should not be ignored.

It is now possible to consider particular cases which reveal not only the correspondence or supplementary nature of the different methods of investigation, but also the relative advantages and disadvantages. The first study will be limited to an analysis of the exact severity of the disease, the degree and site of occlusion, and the degree of compensatory circulation.

### DISCLOSURE OF SEVERITY AND SITE OF THE OCCLUSION

The following five cases are examples of thrombo-angiitis obliterans.

CASE 1.—A man, aged 47 years, had claudication at the arch of the left foot and ulceration of the fifth toe of the left foot. Digital examination (Table II) revealed good femoral pulsations on both sides, but complete absence of pulsation below the left knee. Oscillometry indicated very poor pulsations below the left knee and none in the left foot. The temperature of the left foot was also low. All methods indicated that the right leg was comparatively unaffected.

This case illustrates correspondence in results of different methods.

CASE 2.—A man, aged 38 years, had suffered from intermittent claudication of the calves of both legs for seven years. Two years before he came to the clinic the big toe of the right foot had been amputated elsewhere for gangrenous ulceration.

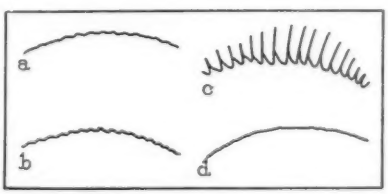


Fig. 2.—Quantitative diagnosis by oscillometric tracings in Case 2: *a*, right ankle; *b*, right foot; *c*, left ankle; *d*, left foot.

Healing had been obtained only after two further amputations, the latter of which was through the head of the metatarsal bone. Subsequently the right foot had given no trouble, but at the time of his visit to the clinic the second toe of the left foot was painfully ulcerated. Digital examination indicated complete absence of pulsation in the posterior tibial and dorsalis pedis arteries of both feet, from which it might be concluded that both extremities were potentially in danger of gangrene. This was not so. Oscillometric studies at the ankle gave evidence of very poor pulsations on the right side (Fig. 2 *a*) and good pulsations on the left (Fig. 2 *c*). In the foot, however, the position was quite reversed; pulsations were of moderate amplitude in the right foot (Fig. 2 *b*) and completely absent in the left (Fig. 2 *d*).

TABLE II

OSCILLOMETRIC AND SPHYGMOMANOMETRIC VALUES IN A CASE OF THROMBO-ANGIITIS OBLITERANS

| SITE | DIGITAL PALPATION, GRADE | | TYCOS APPARATUS | | | | | | PACHON APPARATUS | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | RIGHT | | | LEFT | | | RIGHT | | | LEFT | | |
| | | | BLOOD PRESSURE | | | BLOOD PRESSURE | | | BLOOD PRESSURE | | | BLOOD PRESSURE | | |
| | RIGHT | LEFT | SYSTOLIC | DIASTOLIC | OSCILLOMETRIC UNITS | SYSTOLIC | DIASTOLIC | OSCILLOMETRIC UNITS | SYSTOLIC | DIASTOLIC | OSCILLOMETRIC UNITS | SYSTOLIC | DIASTOLIC | OSCILLOMETRIC UNITS |
| Popliteal region | 4 | 0 | | | | | | | | | | | | |
| Lower border of patella | | | 130 | 85 | 7 | 120 | 85 | 5 | 120 | 80 | 3 | 100 | 60 | 0.5 |
| 5 cm. below patella | | | 130 | 90 | 7 | 115 | 85 | 2 | 150 | 90 | 4 | 130 | 90 | 1 |
| 10 cm. below patella | | | 130 | 90 | 4 | 105 | 80 | 1 | 150 | 110 | 3 | 120 | 100 | 1 |
| Ankle | | | 120 | 85 | 4 | 105 | 85 | 0.5 | 150 | 110 | 2 | 120 | 100 | 0.1 |
| Posterior tibial region | 3 | 0 | | | | | | | | | | | | |
| Dorsalis pedis region | 3 | 0 | | | | | | | | | | | | |
| Foot | | | | | 1.5 | | | | | | | | | |
| Brachial region | | | 130 | 80 | | | | | 140 | 90 | | | | |
| Cutaneous temperature of toes, degrees C. | 32.3 | 29 | | | | | | | | | | | | |

The right foot had been in greatest danger initially; the main arteries were occluded as far up as the calf. This foot, however, was now well nourished by the development of a collateral circulation as shown by the use of the small pneumatic bag, and was not likely to suffer from trophic trouble. The left foot, on the contrary, was threatened with gangrene and the vessels were occluded just above the internal malleolus.

It is obvious that in this case digital examination alone might give an incomplete and erroneous impression. This would also be true of oscillometric measurements limited to the ankle.

CASE 3.—A Roumanian Jew, aged 25 years, had a history of recurrent superficial phlebitis of the left leg over a period of seven months. Evidence of recent and organized superficial phlebitis could be seen on the ankle and leg. Oscillometry revealed very good pulsation at the ankle and foot. Digital examination, however, revealed complete absence of pulsation at the site of palpation of the posterior tibial artery, behind the internal malleolus. The association with recurrent phlebitis rendered the diagnosis of localized thrombo-angiitis obliterans almost certain.

This case illustrates the importance of digital examination.

CASE 4.—A man, aged 34 years, had suffered from intermittent claudication of the left calf for one year, and from coldness and numbness of the left foot for eight months. The popliteal, posterior tibial, and dorsalis pedis arteries in the left leg were closed and pulsations were not recorded at the ankle. The right leg, however, was apparently unaffected, and all the vessels were open. Nevertheless, the surface temperatures of both feet were approximately the same, 29° C., and they gave no indication as to the true state of affairs. After lumbar sympathetic ganglionectomy, the temperature of the right foot was 35° C. and that of the left foot, 34° C.

This case illustrated the inadequacy of surface temperatures for diagnosis. In the majority of cases the surface temperature of an extremity, in which the main vessels are occluded, is lower than that of the sound limb. In these cases surface temperature is of diagnostic value. Apart from the numerous environmental factors which may obscure the significance of a single reading of surface temperature, a very important factor is the superimposed or primary effect of a vasoconstrictor element that may involve both limbs. This may render differentiation by readings of temperature impossible.

CASE 5.—A man, aged 43 years, had suffered from cold feet for several years. Five months before he came to the clinic the fourth toe of the left foot became infected and gangrene developed. Amputation at the base of the toe was successful; the wound healed. For one month the third toe had been persistently ulcerated. The fourth toe on the right foot was cyanotic. On digital examination all the vessels appeared to be open, and this was confirmed by oscillometry; adequate pulsation was obtained even in the foot. Surface temperatures of the toes were all approximately 27° C. Postural tests disclosed slight pallor on elevation of the left foot, but no other changes.

Against the possibility of a purely vasospastic disorder were the following factors: the patient was a male; the gangrene of the left fourth toe was apparently

gangrene of the whole digit and only one toe was cyanotic; the postoperative temperatures were elevated but not maximal. The history and clinical considerations were the chief factors in arriving at a preoperative diagnosis. A modification of the oscillometric test gave a positive result. If the pneumatic bag was placed around the ankle and a pressure of 150 mm. was produced in it, and then the pressure was lowered by 10 mm. at a time, a dusky red color could be produced in some of the toes at a pressure of 110 mm. This localized dusky color does not occur in normal persons, and the test is apparently more sensitive than the dependency postural test, which was negative in this case.

This case illustrated the occasional fallacy of all methods. In cases of patients who present themselves with symptoms or signs of organic occlusion of the arteries of the extremities, it is usual to find the main vessels involved. On this fact depends the importance of digital examination and of oscillometric determinations. If, however, at the time of examination, the digital arteries alone are affected, such methods will give results which in themselves might lead to a fallacious conclusion.

*The Pressure Gradient.*—If determinations of blood pressure are made at the sites at which amplitudes of pulsation are recorded, it will be observed that with partial occlusion of large vessels there is a relation between the blood pressure and the amplitude of pulsation at any given point. In thrombo-angiitis obliterans, or arteriosclerosis with occlusion, the amplitude of pulsation tends to diminish from the knee downward toward the ankle. Coincident with this is a corresponding fall of blood pressure, and this might be termed "the pressure gradient." It is in striking contrast to the measurements in a normal person, in whom the pressure below the knee is approximately constant, down to and including measurements at the level of the ankle. Above the knee, even in a normal case, there is, however, some increase in pressure associated with increased size of arteries.

Fig. 3 shows the pressure gradient and amplitudes of pulsation in a case of arteriosclerosis compared with corresponding values for a normal person. The data given in the preceding cases of thrombo-angiitis obliterans disclose the same phenomena.

*The Occult Blood Pressure.*—If no record of pulsations or of blood pressure can be obtained at the right ankle, this does not necessarily mean that there is no blood flowing through the large vessels at this point. If the foot is blanched by elevation, and the pressure in a pneumatic bag around the ankle is raised above the anticipated normal pressure, then when the limb is lowered to the horizontal position and the pressure in the bag is gradually decreased by 10 mm. at intervals of two minutes, a point will be reached at which the foot is seen to become red. This indicates the pressure that is just inadequate to suppress the flow of blood to the foot at the point of measurement, the ankle, and might be termed the "occult blood pressure."

*Comment.*—The value of oscillometry in quantitative diagnosis of peripheral vascular disease is considerable. Quantitative diagnosis infers the complete elucidation of the exact degree and site of the disease. The Pachon apparatus and the Tycos apparatus are both suitable instruments, but the latter is of greater value in furnishing permanent and indisputable records and in lending itself more readily to examination of smaller and more distal regions. The latter examinations are often of great significance and may be the key to the condition.

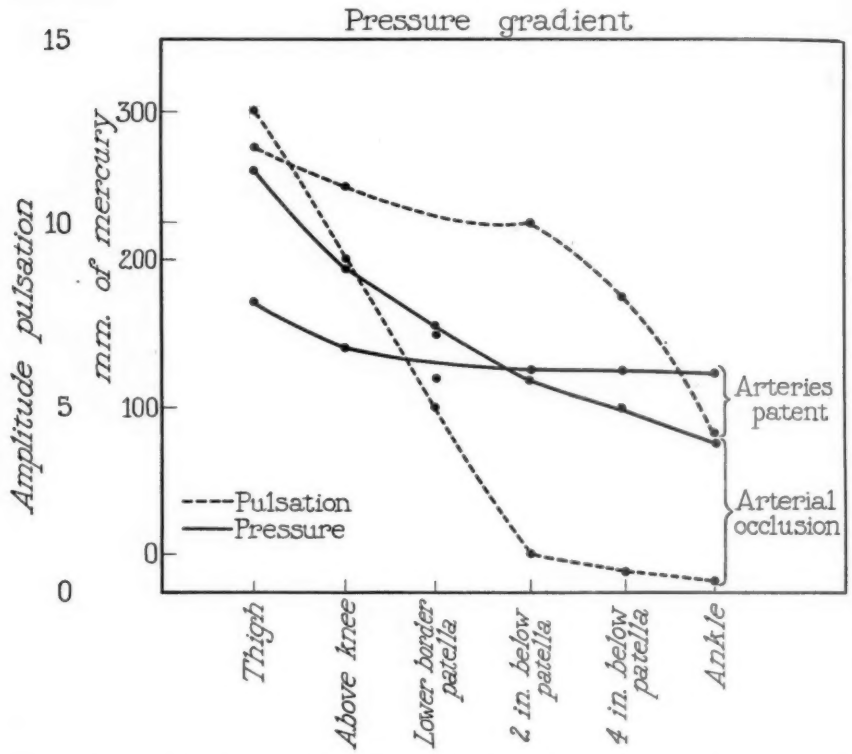


Fig. 3.—Pressure gradient and amplitude of pulsation in a case of arteriosclerosis compared with corresponding values for a normal person.

Digital examination is extremely useful and should not be dispensed with. In skilled hands it may give results as useful as those given by oscillometry, but for the average observer digital examination alone will not be used with the confidence or certainty with which oscillometry can be employed. Surface temperatures are not of great value for quantitative diagnostic purposes, although their importance in the complete study of vascular disease cannot be overemphasized. Clinical studies, postural and similar tests, all play an important part in diagnosis, and oscillometry is not intended to replace, but to supplement, other methods of investigation.

OSCILLOMETRIC STUDIES IN VACCINE FEVER

The response to fever produced by intravenous administration of typhoid vaccine has been used by Brown as an important factor in determining the suitability of cases of thrombo-angiitis obliterans for lumbar sympathetic ganglionectomy. His vasomotor index is determined after the temperature has been caused to rise by the vaccine and consists in the result of calculating as follows: the difference between the rise in temperature of the mouth and in the surface temperature

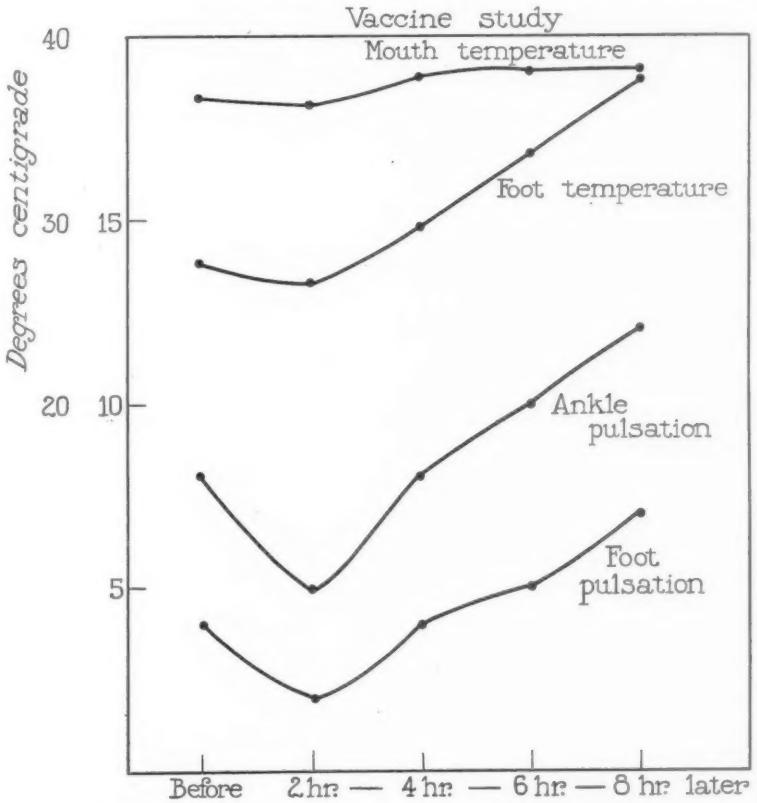


Fig. 4.—Effect of vaccine fever on temperature and pulsation.

of the foot, divided by the rise in temperature of the mouth.* An index of 2 or more has been taken to indicate a large element of spasm. Further vaccine fever produced at intervals of a few days often itself constitutes an important therapeutic measure. The present study was carried on to determine whether oscillometric readings (1) were definitely related to increased cutaneous temperature, (2) were of prognostic value, or (3) gave any indication of the potentiality of arteries to increase their amplitude of pulsation.

*The absolute increase in surface temperature with fever may be as satisfactory an index.

In order better to understand the mechanism of vaccine fever, preliminary studies were made in cases of polyarthritis in which the blood vessels were presumably free from organic disease, and therefore not limited in their power to respond.

*Arthritis.*—From Fig. 4 and Table III it will be seen that the amplitude of pulsation both at the ankle and at the foot appears to bear a direct relationship to the cutaneous temperature during vaccine fever. Although the increased amplitude of pulsation is associated with a rise in oral temperature, the correspondence is not maintained; cutaneous temperature and amplitude of pulsation continue to increase after the oral temperature has attained its maximal value. When there is a large vasospastic element, the oral temperature might rise as much as 2° C. without, at first, any gross change in the cutaneous temperature. Then, after five or six hours, with striking suddenness, both the cutaneous temperature and the amplitude of pulsation soar to a maximum, as if a controlling mechanism had been abruptly released.

TABLE III

OSCILLOMETRIC VALUES IN A CASE OF ARTHRITIS IN WHICH FEVER WAS INDUCED BY THE ADMINISTRATION OF VACCINE

| TIME | TEMPERATURE, DEGREES C. | | OSCILLOMETRIC UNITS, TYCOS | |
|---|---|---|---|---|
| | ORAL | FOOT | ANKLE | FOOT |
| Before vaccine | 36.7 | 27.7 | 8 | 4 |
| After vaccine, hours | | | | |
| 2 | 36.3 | 26.8 | 5 | 2 |
| 4 | 37.8 | 29.6 | 8 | 4 |
| 6 | 38.0 | 33.7 | 10 | 5 |
| 8 | 38.0 | 37.7 | 12 | 7 |

It will be seen from Fig. 4 that in the first hour or two following the intravenous administration of vaccine there was a correlated fall in all measurements. This was associated with a sense of chilliness. If more frequent measurements are taken, it will be seen in some cases that there is a slight rise in cutaneous temperature and in oscillations before the fall. With larger doses of vaccine, especially in a hypersensitive person, definite rigor may occur and the prodromal phase may be much more marked. In some cases the foot becomes very cold and the pulsation at the ankle and foot may disappear. In cases of arteriosclerotic disease this, in rare instances, may be the cause of further thrombosis. It is thus advisable to avoid prolonged rigor. Barker has shown the value of typhoid "H" antigen for producing fever with little, if any, chill.

Some cases of arthritis have a large vasospastic element, and in these cases the pulsation of the foot or finger before vaccine is given may be minimal, and the resulting increased amplitude of pulsation very striking (Fig. 5).

*Thrombo-angiitis Obliterans.*—It has already been seen from the diagnostic studies that cutaneous temperatures are not necessarily an indication of the degree of patency or amplitude of pulsation of main arteries. This is due to the fact that the more immediate regulation of cutaneous temperature is the peripheral vasomotor mechanism which affects arterioles. Nevertheless, in many cases occlusion of main arteries is associated with diminution of cutaneous temperature. These considerations are further elucidated by a study of oscillometric tracings and cutaneous temperatures during vaccine fever in cases of thrombo-angiitis obliterans.

In Case 4 the left leg was chiefly involved; pulsation in the left ankle and foot were absent under ordinary circumstances, and those on the right side were good. Observations were made with both small and large doses of vaccine. With a dose of 25,000,000 bacilli the oral

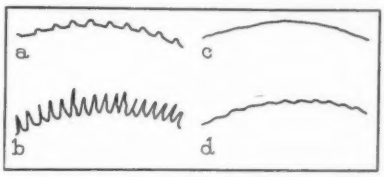


Fig. 5.—Effect of vaccine fever on oscillometric tracing in a case of arthritis: *a*, foot before fever; *b*, foot in course of fever; *c*, finger before fever; and *d*, finger in course of fever.

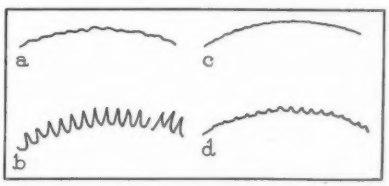


Fig. 6.—Effect of vaccine fever on oscillometric tracing in a case of thrombo-angiitis obliterans: *a*, right foot before fever; *b*, right foot in course of fever; *c*, left foot before fever, and *d*, left foot in course of fever.

temperature rose only to 37.2° C., but the cutaneous temperature of the right foot rose 9.2° C., from 25.6° to 34.8° C. Pulsations at the right ankle and right foot (Fig. 6) were actually doubled in amplitude. With a dose of 75,000,000 bacilli and a resulting oral temperature of 38.9° C., the cutaneous temperature was 34.8° C. There is, therefore, no constant proportionate relationship between oral and cutaneous temperatures, although with the ultimate oral temperature of 40.1° C. the cutaneous temperature rose to 36.7° C. The amplitude of pulsation in the right ankle was no greater at this high temperature than at 37.2° C., but that of the foot was still further increased. Pulsations in the foot are more closely related to cutaneous temperature of the foot than those in the ankle. In thrombo-angiitis obliterans pulsation may be constant, with marked variations in cutaneous temperature.

If one examines the sequence of events in the left leg of this patient, some interesting points are disclosed. In the first instance, with normal oral temperature, pulsation both at the ankle and foot (Fig. 6) was completely absent. Yet the initial cutaneous temperature was even a little higher than that on the right foot (left, 26.1° C.; right, 25.6° C.). With fever, the cutaneous temperature rose 9.9° C., almost as wide a range as that of the right foot (11.1° C.); yet the pulsations that appeared at the ankle and foot were minimal (Fig. 6). Thus the effect of occlusion of main vessels does not necessarily prevent a considerable rise of cutaneous temperature; the latter is dependent on the ability of the arterioles to dilate fully, and presumably on the presence of adequate collateral circulation.

In contrast to the case just described, a case of thrombo-angiitis obliterans (Case 1) will be considered, in which the vasomotor index was poor and operation was contraindicated. The left leg was the one affected, and is the one which will therefore be considered here. With a dose of 125,000,000 bacilli, for the patient was refractory to smaller doses, the oral temperature rose 1.8° C. The cutaneous temperature, however, increased only from 28.7° C. to 32.6° C.; the vasomotor index was poor in this limb, namely, 1.2° C. The minimal pulsations at the ankle were hardly affected by the vaccine fever, whereas those at the foot were persistently absent. It is not uncommon for a poor index to be associated with persistent absence of pulsation in the foot, even at the height of fever. The latter, however, is not of absolute prognostic value, for a relative increase of cutaneous temperature may be obtained in the persistent absence of pulsation in the foot. It may be said, however, that under these circumstances the postoperative temperature of the skin rarely attains values greater than about 32.5° C. and is more often less than that. On the other hand, in the presence of good pulsation in the foot, at the height of fever, the postoperative surface temperature probably will be in the neighborhood of 34° C.

*Comment.*—The foregoing studies indicate the rôle of oscillometry in determining the potentiality of arteries to dilate. When an artery is capable of dilatation, there is usually a relationship between temperature of the skin and amplitude of pulsation; this is much more true of the foot than of the ankle. The presence or increase of pulsation in the foot at the height of fever is of some prognostic value as to effects of ganglionectomy. Oscillometric measurements during fever give some indication as to the potentiality of arteries to increase their amplitude of pulsation. Studies of surface temperature are here of greater prognostic significance than oscillometric measurements.

### VASCULAR STUDIES IN RELATION TO LUMBAR SYMPATHETIC GANGLIONECTOMY

*Direct Study of Vasomotor Mechanism.*—If an increase in amplitude of pulsation of peripheral arteries is to be considered as a possible therapeutic index, it is important to determine whether direct paraly-

sis or stimulation of a vasomotor nerve can affect such amplitude. Local anesthesia of the ulnar nerve at the elbow produced a rise of temperature in the little finger and a very marked increase in the amplitude of pulsation of the digital artery (Fig. 7 *a* and *b*). Similar results were obtained in the foot and even the ankle following spinal anesthesia. Mechanical stimulation of the fourth lumbar ganglion in man, during operation, produced marked diminution in the amplitude of pulsation at the foot and at the ankle (Fig. 8 *a* and *b*). It is concluded that vasomotor nerves can influence the amplitude of pulsation of peripheral arteries.

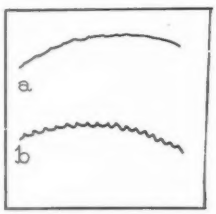


Fig. 7.

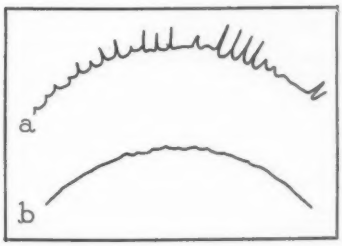


Fig. 8.

Fig. 7.—(*a*), Digital pulsation before anesthetization of ulnar nerve; (*b*), digital pulsation after anesthetization of ulnar nerve.

Fig. 8.—Mechanical stimulation of fourth lumber ganglion: *a*, intermittent; *b*, constant.

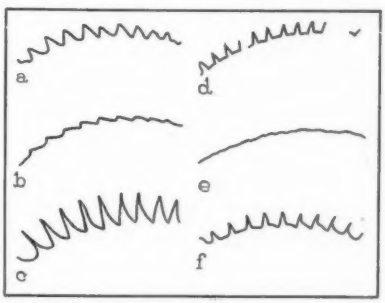


Fig. 9.—Stimulation of foot after lumbar sympathetic ganglionectomy. A case of arthritis: *a*, exposure to atmosphere; *b*, immersion in cold water, and *c*, immersion in hot water. A case of thrombo-angiitis obliterans: *d*, exposure to atmosphere; *e*, immersion in cold water, and *f*, immersion in hot water.

*Effect of Stimulation on Denervated Vessels.*—The object of this investigation was to decide whether certain stimuli could affect the tone of an artery after severance of the vasomotor nerve. Cases of Raynaud's disease, arthritis, and Buerger's disease were studied at varying intervals after operation, from three weeks to five years. In all cases immersion of the foot in cold water (15° C.) for twenty to thirty minutes produced considerable diminution in amplitude of pulsation. This was most marked in the case of thrombo-angiitis obliterans, possibly because of the pathological state of the artery. Hot water (42° C.) for thirty minutes produced increased amplitude of pulsation (Fig. 9).

The complete severance of vasomotor nerves in these cases was shown by negative sweating tests. It is therefore concluded that heat and cold can probably act directly on the arterial wall.

*Instrumental and Palpatory Methods.*—Many workers in the field of peripheral vascular disease have cited increased amplitude of pulsation at the ankle as evidence in support of the value of a therapeutic procedure, medical or surgical. The failure to increase this amplitude similarly has been tacitly accepted as a negative or adverse result. It was therefore important to estimate accurately the value of oscillometry as a therapeutic index. The evidence obtained and considered

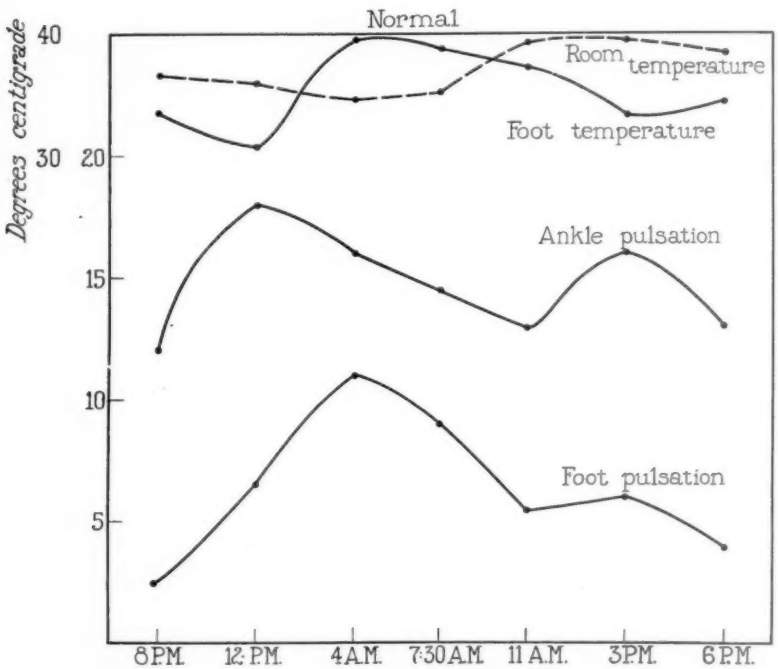


Fig. 10.—Physiological variations in pulsation in twenty-four hours in a normal person.

fully indicates that the assumptions just mentioned were often unjustified and took no account of numerous physiological variations. Oscillometric measurements in the foot, however, are of some relative value. Surface temperature will be seen to be of the greatest importance in estimating the effect of therapeutic procedures. Whereas it is usually recognized that surface temperatures must be taken under standard or controlled conditions, oscillometric measurements are nearly always recorded with complete disregard of such factors.

*Physiological Variations.*—Oscillometric measurements in ankle, foot and arm have been taken at intervals of approximately three hours throughout the day and night, and simultaneous readings of surface

temperature, room temperature, mouth temperature, pulse, and blood pressure have been made. Normal subjects, and patients with peripheral vascular disease have been studied, the latter before and after lumbar sympathetic ganglionectomy. The technical procedure was similar in all cases; surface temperatures were taken after the foot had been exposed to the atmosphere of the room for ten minutes.

The results in a normal adult are given in Table IV and Fig. 10, from which it will be seen that there is considerable variation in the amplitude of pulsation. The factors entering into this variation are complex and do not appear to lend themselves to exact analysis. It is obvious, however, that the unqualified statement of a preoperative oscillometric value is meaningless and does not offer any standard for subsequent comparison. The variation in the amplitude of pulsation is not constant for all persons, any more than do hourly readings of blood pressure give constant curves in all cases, or even for the same patient on successive days. Nevertheless in the cases investigated,

TABLE IV

PHYSIOLOGICAL VARIATION OF OSCILLOMETRIC AND SPHYGMOMANOMETRIC VALUES IN TWENTY-FOUR HOURS IN A NORMAL ADULT

| TIME | RIGHT ANKLE | | | RIGHT FOOT | | ARM | | | | TEMPERATURE, DEGREES C. | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | BLOOD PRESSURE | | OSCILLOMETRIC UNITS, TYCOS | OSCILLOMETRIC UNITS, TYCOS | TEMPERATURE, DEGREES C. | BLOOD PRESSURE | | OSCILLOMETRIC UNITS, TYCOS | PULSE, BEATS EACH MINUTE | | |
| | SYSTOLIC | DIASTOLIC | | | | SYSTOLIC | DIASTOLIC | | | ORAL | ROOM |
| 8:00 P.M. | 145 | 85 | 12 | 3.5 | 31.8 | 135 | 80 | 13 | 80 | 36.8 | 23.3 |
| 12:00 M. | 165 | 90 | 18 | 6.5 | 30.4 | 150 | 90 | 20 | 75 | 36.7 | 23.0 |
| 4:00 A.M. | 160 | 85 | 16 | 11 | 34.8 | 145 | 90 | 22 | 80 | 36.8 | 22.3 |
| 7:30 A.M. | 170 | 100 | 14.5 | 9 | 34.4 | 155 | 95 | 30 | 66 | 36.7 | 22.6 |
| 10:30 A.M. | 160 | 90 | 13 | 5.5 | 33.6 | 130 | 90 | 15 | 72 | 36.8 | 24.6 |
| 3:00 P.M. | 140 | 90 | 16 | 6 | 31.7 | 125 | 70 | 26 | 81 | 36.9 | 24.7 |
| 6:00 P.M. | 160 | 95 | 13 | 4 | 32.2 | 140 | 80 | 16 | 84 | 37.0 | 24.2 |

the tendency to diurnal variations manifested itself. Pulsations in the foot appear to have some relationship to the surface temperatures, although this is not necessarily the case. Pulsations at the ankle are seen in Fig. 10 to be somewhat dissociated from the variation in surface temperature. This is only to be expected, for surface temperature is largely determined by a peripheral vasomoter mechanism which affects arterioles, whereas pulsations of the ankle are probably influenced in a greater degree by the state of the systemic circulation. Table V and Fig. 11 illustrate observations for twenty-four hours before lumbar sympathetic ganglionectomy in Case 4, an example of thrombo-angiitis obliterans.

Table VI and Fig. 12 show the results of observations in the same case three weeks after lumbar sympathetic ganglionectomy. The oscillometric curves are much flatter than they were before operation, indi-

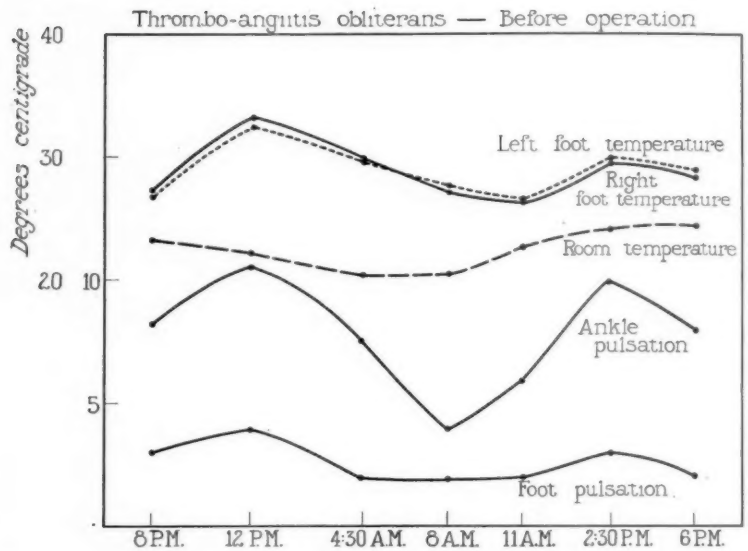


**Fig. 11.—Observations for twenty-four hours before lumbar sympathetic ganglionectomy in a case of thrombo-angiitis obliterans.**

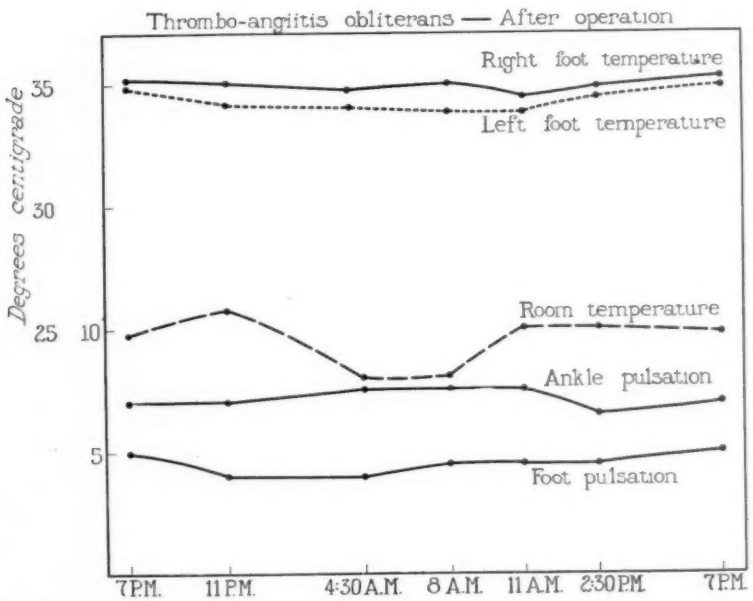


**Fig. 12.—Observations over a period of twenty-four hours, three weeks after lumbar sympathetic ganglionectomy in the same case of thrombo-angiitis obliterans as that from which Fig. 11 was made.**

cating less variation throughout the day. Observation in other cases, including cases of arthritis but not including any cases of organic arterial disease, indicates that this is usually so, although it is by no means always as marked as in this instance. Control postoperative observations made on patients with normal vascular systems, but with other lesions such as gastric ulcer, show that there are considerable variations throughout twenty-four hours. The most significant feature seen after sympathetic ganglionectomy is the persistent and almost invariable high surface temperature throughout the twenty-four hours. The values are markedly and constantly higher than before operation, and indicate the extreme importance of surface temperature as a therapeutic index. Further, this constantly high surface temperature has been found to persist in cases in which operation had been done five years before.

By comparing oscillometric readings in Case 4 at similar times of the day, it is seen that there is no postoperative increase in pulsation at the ankle; in fact, at many points there is an apparent decrease. In the right foot, however, there is a definite and fairly constant increase in amplitude of pulsation, and in the left foot pulsations have appeared which were absent before operation, except during the vaccine fever that was induced preoperatively. The latter point appears to be of prognostic value, intimating not only a relative increase of surface temperature, but an absolutely high temperature, usually greater than 32.5° C. It will be noted that postoperative temperatures are almost equal in the right and left leg in spite of the marked differences in pulsation between the limbs.

The vasomotor index in this case was good, greater than 2, and the temperatures attained in the two extremities during vaccine fever were, respectively, 34.8° and 34.9° C., a close approximation to the postoperative surface temperatures. On another occasion, however, with a higher dose of vaccine, the oral temperature rose to 40.1° C. and the temperatures of the feet to 36.7° and 36° C., respectively. This illustrates the fact that an oral temperature greater than 38.5° or 39° C. may not be optimal for prognostic purposes; the surface temperatures then may be in excess of their postoperative values.

*The Immediate Postoperative Period.*—During the first six hours or so after periarterial sympathectomy a negative phase* occurs (Leriche) in which both the temperature and the amplitude of oscillation are considerably less than that previous to operation. This has been attributed to irritative stimulation of the periarterial sympathetic plexus

*Following the negative phase, after operation there is a hyperactive phase, during which time all values are in excess of their ultimate attainment. It is perhaps analogous to the "reactionary phase" of Leriche but probably of different mechanism. The effect of general anesthesia cannot be ignored. Further, the hyperactive phase is almost always associated with some degree of postoperative fever. However, the higher oscillometric values may persist for a few days after the oral temperature has returned to normal. The vessels recover their normal pulsations toward the end of the first week.

TABLE V

OSCILLOMETRIC AND SPHYGMOMANOMETRIC VALUES FOR TWENTY-FOUR HOURS BEFORE LUMBAR SYMPATHETIC GANGLIONECTOMY IN A CASE OF THROMBO-ANGIITIS OBLITERANS, CASE 4

| TIME | RIGHT ANKLE | | | RIGHT FOOT | | LEFT ANKLE | LEFT FOOT | | BRACHIAL | | | PULSE, BEATS EACH MINUTE | TEMPERATURE, DEGREES C. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | BLOOD PRESSURE | | OSCILLOMETRIC UNITS, TYCOS | OSCILLOMETRIC UNITS, TYCOS | TEMPERATURE, DEGREES C. | OSCILLOMETRIC UNITS, TYCOS | OSCILLOMETRIC UNITS, TYCOS | TEMPERATURE, DEGREES C. | BLOOD PRESSURE | | OSCILLOMETRIC UNITS, TYCOS | | ORAL | ROOM |
| | SYSTOLIC | DIASTOLIC | | | | | | | SYSTOLIC | DIASTOLIC | | | | |
| 8:00 P.M. | 145 | 90 | 8.25 | 3 | 27.3 | 1.5 | 0 | 26.8 | 120 | 80 | 12 | 60 | 36.7 | 23.3 |
| 12:00 M. | 120 | 75 | 10.5 | 4 | 31.6 | 2 | 0 | 31.4 | 110 | 70 | 12 | 54 | 35.9 | 22.1 |
| 6:30 A.M. | 130 | 80 | 7.5 | 2 | 29.6 | 1 | 0 | 29.8 | 125 | 80 | 13 | 52 | 36.0 | 20.4 |
| 8:00 A.M. | 145 | 90 | 4 | 2 | 27.2 | 1 | 0 | 27.5 | 135 | 90 | 11 | 60 | 36.8 | 20.5 |
| 11:00 A.M. | 145 | 100 | 6 | 2 | 26.4 | 1.5 | 0 | 26.5 | 130 | 80 | 9 | 60 | 36.9 | 22.8 |
| 2:30 A.M. | 135 | 85 | 10 | 3 | 29.5 | 2 | 0 | 30.0 | 130 | 80 | 19 | 60 | 36.7 | 24.2 |
| 6:00 P.M. | 140 | 90 | 8 | 2 | 28.4 | 2 | 0 | 28.7 | 142 | 90 | 16 | 56 | 36.8 | 24.4 |

TABLE VI

OSCILLOMETRIC AND SPHYGMOMANOMETRIC VALUES FOR TWENTY-FOUR HOURS, THREE WEEKS AFTER LUMBAR SYMPATHETIC GANGLIONECTOMY IN A CASE OF THROMBO-ANGIITIS OBLITERANS, CASE 4

| TIME | RIGHT ANKLE | | | RIGHT FOOT | | LEFT ANKLE | LEFT FOOT | | ARM | | | PULSE, BEATS EACH MINUTE | TEMPERATURE, DEGREES C. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | BLOOD PRESSURE | | OSCILLOMETRIC UNITS, TYCOS | OSCILLOMETRIC UNITS, TYCOS | TEMPERATURE, DEGREES C. | OSCILLOMETRIC UNITS, TYCOS | OSCILLOMETRIC UNITS, TYCOS | TEMPERATURE, DEGREES C. | PRESSURE BLOOD | | OSCILLOMETRIC UNITS, TYCOS | | ORAL | ROOM |
| | SYSTOLIC | DIASTOLIC | | | | | | | SYSTOLIC | DIASTOLIC | | | | |
| 7:00 P.M. | 125 | 90 | 7 | 5 | 35.2 | 2 | 0.5 | 34.8 | 125 | 80 | 16 | 70 | 37.0 | 24.8 |
| 11:00 P.M. | 120 | 80 | 7 | 4 | 35.0 | 1.5 | 0.5 | 34.1 | 115 | 75 | 14 | 64 | 37.0 | 25.8 |
| 4:30 A.M. | 120 | 80 | 7.5 | 4 | 34.8 | 2 | 0.5 | 34.0 | 130 | 80 | 11 | 70 | 36.5 | 23.0 |
| 8:00 A.M. | 150 | 100 | 7.5 | 4.5 | 35.0 | 1 | 0.5 | 33.8 | 140 | 90 | 12 | 72 | 36.9 | 23.1 |
| 11:00 A.M. | 135 | 90 | 7.5 | 4.5 | 34.4 | 1.5 | 0.5 | 33.8 | 130 | 90 | 9 | 70 | 36.9 | 25.0 |
| 2:30 P.M. | 135 | 90 | 6.5 | 4.5 | 34.8 | 2 | 0.5 | 34.4 | 135 | 90 | 12 | 70 | 37.0 | 25.0 |

and is followed by a positive phase of recovery and transitory overcompensation. Observations were carried out to determine whether such phenomena occur with lumbar sympathetic ganglionectomy.

TABLE VII

OSCILLOMETRIC AND SPHYGMOMANOMETRIC VALUES IN A CASE OF THROMBO-ANGIITIS OBLITERANS IMMEDIATELY AFTER AND REMOTELY AFTER LUMBAR SYMPATHETIC GANGLIONECTOMY

| TIME | TEMPERATURE, DEGREES C. | | ANKLE BLOOD PRESSURE | | ANKLE OSCILLOMETRIC UNITS, TYCOS | ARM BLOOD PRESSURE | | ROOM TEMPERATURE, DEGREES C. |
|---|---|---|---|---|---|---|---|---|
| | ORAL | FOOT | SYSTOLIC | DIASTOLIC | | SYSTOLIC | DIASTOLIC | |
| Before operation | 36.9 | 27.5 | 105 | 70 | 3 | 155 | 95 | 25.2 |
| After operation, hours | | | | | | | | |
| 1 | 35.0 | 29.2 | | | 0.1 | 100 | 70 | 24.4 |
| 3 | 35.6 | 29.8 | | | 0.1 | 112 | 70 | 24.6 |
| 7 | 36.7 | 30.6 | | | 0.5 | 120 | 76 | 25.2 |
| 10 | 37.0 | 30.9 | | | 1 | 130 | 80 | 24.8 |
| 13 | 37.2 | 31.2 | 100 | 70 | 2.5 | 140 | 90 | 24.4 |
| Day after operation | 37.2 | 32.6 | 100 | 70 | 3 | 145 | 90 | 25.0 |
| Three weeks later | 36.9 | 31.9 | 105 | 70 | 3 | 145 | 85 | 25.0 |

Table VII gives the data for a case of thrombo-angiitis obliterans which occurred in a man, aged fifty-three years, whose right leg had been amputated some years previously. It is seen that there was an immediate fall in amplitude of pulsation at the left ankle following lumbar sympathetic ganglionectomy and disappearance of pulsation in the foot; recovery commenced seven hours later. The chief cause of this, however, appears to have been a state of mild shock, for there was a corresponding fall of blood pressure and a subnormal oral temperature. This view was further confirmed by the occurrence, on the seventh day, of temporary unexplained jaundice associated with some degree of collapse. The pulsation in the ankle again almost disappeared, but attained a supernormal value following intravenous administration of saline solution. The cutaneous temperature was always greater than before operation, but there was a relatively negative phase since this temperature gradually increased with the increase of pulsation and recovery from shock. Pulsation in the foot in this case was minimal and did not increase either after operation or administration of vaccine. The final postoperative temperature was 31.9° C., as compared with the postvaccinal temperature of 32° C.

Apart from the major influence of shock, there may be a direct factor of irritation of nerves, for studies in the operating room tended to show that severe mechanical manipulation of lumbar ganglia was not followed by immediate complete recovery of the amplitude of pulsation.

*Later Postoperative Period.*—Oscillometric studies and observations of temperature were carried out daily throughout the postoperative period in a case of thrombo-angiitis obliterans in which the patient, a man, was aged forty-two years. The disease affected chiefly the left leg.

Table VIII gives the essential data. It will be seen that there was an immediate negative phase as described in Case 9, but the phase of recovery was more rapid. After five hours pulsation appeared in the left foot. This was completely absent before operation except at the height of the vaccine fever. The pulsations attained their maximal degree on the first day and then gradually disappeared on the seventh

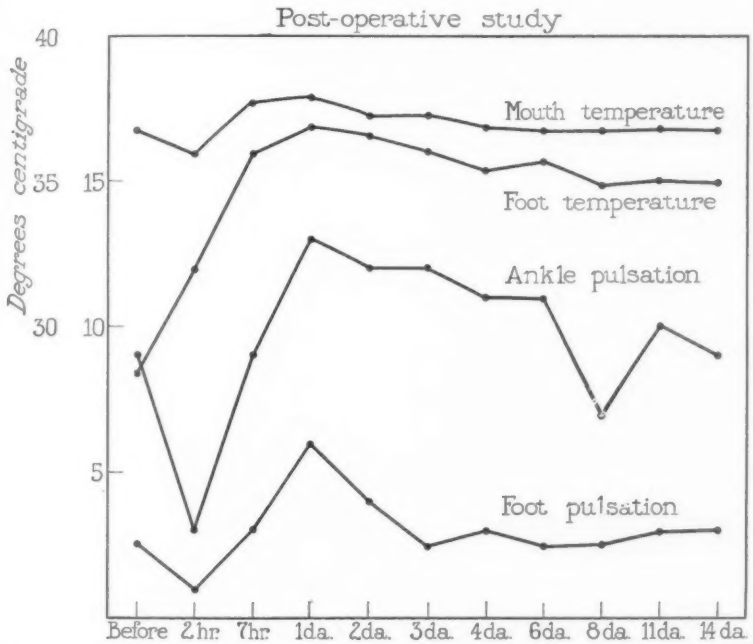


Fig. 13.—Observations before and after lumbar sympathetic ganglionectomy in a case of thrombo-angiitis obliterans.

day. Pulsations in the other foot followed a similar course, but were persistently present. Pulsations at the ankle were more variable, but oscillometric measurements on the whole gave little, if any, indication of the ultimate benefit of the operation (Fig. 13). The final temperatures of the skin, however, were 34.9° and 32.8° C. The good vasomotor index was completely justified.

It has been seen from these studies that the occurrence or increase of pulsations in the foot during vaccine therapy is of good prognostic significance, the ultimate postoperative temperature then probably exceeding 32.5° C. A further case of thrombo-angiitis obliterans will be cited to show that in spite of complete and persistent absence of pul-

TABLE VIII

OSCILLOMETRIC AND SPHYGMOMANOMETRIC OBSERVATIONS AFTER LUMBAR SYMPATHETIC GANGLIONECTOMY IN A CASE OF THROMBO-ANGIITIS OBLITERANS

| TIME | RIGHT ANKLE | | | RIGHT FOOT | RIGHT TOE | LEFT ANKLE | | | LEFT FOOT | TEMPERATURE, DEGREES C. | | PULSE BEATS, EACH MINUTE | BRACHIAL BLOOD PRESSURE | | ROOM TEMPERATURE, DEGREES C. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | BLOOD PRESSURE | | OSCILLOMETRIC UNITS, TYCOS | OSCILLOMETRIC UNITS, TYCOS | TEMPERATURE, DEGREES C. | BLOOD PRESSURE | | OSCILLOMETRIC UNITS, TYCOS | OSCILLOMETRIC UNITS, TYCOS | LEFT TOE | ORAL | | SYSTOLIC | DIASTOLIC | |
| | SYSTOLIC | DIASTOLIC | | | | SYSTOLIC | DIASTOLIC | | | | | | | | |
| Before operation | 130 | 90 | 9 | 2.5 | 28.4 | 110 | 60 | 2.5 | 0 | 27.8 | 36.7 | 76 | 120 | 80 | 25.2 |
| After operation, days | | | | | | | | | | | | | | | |
| 2 (hours) | 80 | 60 | 3 | 1 | 32.0 | 70 | 50 | 0.5 | 0 | 29.5 | 35.9 | 100 | 110 | 70 | 26.0 |
| 5 (hours) | 90 | 60 | 6 | 1 | 34.8 | 80 | 50 | 1 | 0.1 | 33.5 | 36.2 | 88 | 118 | 80 | 26.2 |
| 7 (hours) | 120 | 80 | 9 | 3 | 35.9 | 100 | 70 | 4 | 0.5 | 33.4 | 37.6 | 82 | 120 | 80 | 25.6 |
| 1 | 150 | 90 | 13 | 6 | 36.8 | 120 | 70 | 3 | 0.75 | 34.1 | 37.8 | 100 | 116 | 80 | 23.0 |
| 2 | 140 | 90 | 12 | 4 | 36.5 | 120 | 70 | 5 | 0.5 | 34.3 | 37.2 | 72 | 140 | 90 | 26.0 |
| 3 | 130 | 80 | 12 | 2.5 | 35.5 | 110 | 70 | 3.5 | 0.5 | 33.6 | 37.2 | 68 | 130 | 80 | 25.8 |
| 4 | 130 | 80 | 11 | 3 | 35.3 | 110 | 70 | 2.5 | 0.1 | 33.6 | 36.8 | 68 | 120 | 80 | 23.4 |
| 6 | 130 | 80 | 11 | 2.5 | 35.6 | 110 | 70 | 3 | 0.1 | 33.6 | 36.7 | 72 | 115 | 70 | 26.0 |
| 8 | 120 | 80 | 7 | 2.5 | 34.8 | 110 | 70 | 3 | 0 | 33.1 | 36.7 | 66 | 120 | 80 | 25.9 |
| 11 | 130 | 85 | 10 | 3 | 35.0 | 110 | 70 | 2.5 | 0 | 32.8 | 36.7 | 72 | 120 | 80 | 24.0 |
| 14 | 130 | 90 | 9 | 3 | 34.9 | 110 | 70 | 2.5 | 0 | 32.8 | 36.7 | 72 | 120 | 80 | 24.8 |

sations in the foot, a good clinical result can be obtained, associated with relative improvement in surface temperature. The preoperative temperature in the left foot was 24.2° C., the temperature after vaccine had been given was 32° C., the vascular index was greater than 2, and the ultimate postoperative temperature was 31° C. The clinical result was good; an intractable and indolent ulcer healed completely, and the patient was relieved of pain. Although the final temperature was only 31° C., the good vascular index was a reliable indication, since the relative increase in temperature was no less than 6.8° C. and the clinical result was excellent.

*Postoperative Observations in a Case of Arthritis; a Control Study.*—Since the previous study of thrombo-angiitis obliterans was subject to the comment that the arteries concerned were diseased, the following case of arthritis is of interest. The patient was a woman, aged twenty-six years, with arthritis in the hands and feet. The extremities were cold and clammy, and the vascular index was good. Oscillometric measurements were recorded at 2:30 P.M. and at an atmospheric temperature of 25° C. Tracings obtained at the foot, before operation, on the fourth day after operation (temperature 100.2° C.), and three weeks after operation, revealed that there was no ultimate increase in amplitude, although the preoperative surface temperature was 25.8° C., and the postoperative, 36° C. This shows the marked superiority of surface temperatures as a therapeutic index and the enormous potential variation of cutaneous temperature, with constant amplitude of pulsation in the arteries. The amplitude of pulsations at the ankle in this case was actually less than before operation. The pulse, however, after operation tended to be slightly rapid; the rate was 92.

*Comment.*—Oscillometry as frequently practiced is entirely useless as a therapeutic index. Even with stated conditions of examinations, oscillometric values at the ankle tend to have a deceptive value owing to the difficulty of controlling all the physiological influencing factors. Similar comments are applicable, but apparently with less force, to pulsations in the foot. Not infrequently these are persistently greater than preoperative values, but this is by no means necessarily the case even with a considerable increase of surface temperature. Amplitude of pulsation is most likely to increase in such cases if there is a degree of spasm of the dorsalis pedis artery prior to operation.

The limited value of oscillometry as a therapeutic index is due to the fact that the chief action of the vasoconstrictor mechanism is on arterioles and not on arteries. The release of tonus of the arterioles is best detected by the measurement of surface temperature, which is a far better therapeutic index than oscillometry.

## SUMMARY AND CONCLUSIONS

1. The relative value of mechanical methods of diagnosis in peripheral vascular disease is considered. The evidence shows that oscillometry is of value in determining the presence and amplitude or absence of pulsation.

2. The physiology and mechanism of vaccine fever is considered. Its prognostic value is found to be sound, and the vasomotor index seems to be the best single method of expressing it. Oscillometry in the foot during vaccine fever appears to have some prognostic value.

3. Stimulation and paralysis of vasomotor nerves affect arteries as well as arterioles.

4. Local hot and cold stimuli affect the amplitude of pulsation of peripheral arteries even after sympathetic ganglionectomy.

5. Results are reported of studies of physiological variation of amplitude of oscillations in normal conditions and in conditions of disease, throughout twenty-four hours. The variations are such as to render any single reading of little significance. The vasomotor mechanism can vary independently of amplitude of pulsation; the latter is considerably modified by general circulatory factors. Pulsations at the ankle are of little, if any significance as a therapeutic index. Pulsations in the foot are of some value as a therapeutic index.

6. Surface temperature is easily the best single therapeutic index. After sympathetic ganglionectomy surface temperature is found to be persistently high throughout day and night. This appears to be true for an indefinite period of years.

7. Oscillometry is of great value in the physiological study of pulsations in the larger peripheral arteries.

# THE CLINICAL SIGNIFICANCE OF COMPLETE INVERSION OF LEAD III OF THE HUMAN ELECTROCARDIOGRAM

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ALTHOUGH inversion of all the deflections (P, QRS, and T) in Lead III of the human electrocardiogram (Fig. 1) is occasionally encountered, its clinical significance has not been sufficiently appreciated. Unlike most electrocardiographic findings, it is one that has largely escaped analysis and discussion. For comparison it is of interest to note that inversion of all complexes in Lead I has long been

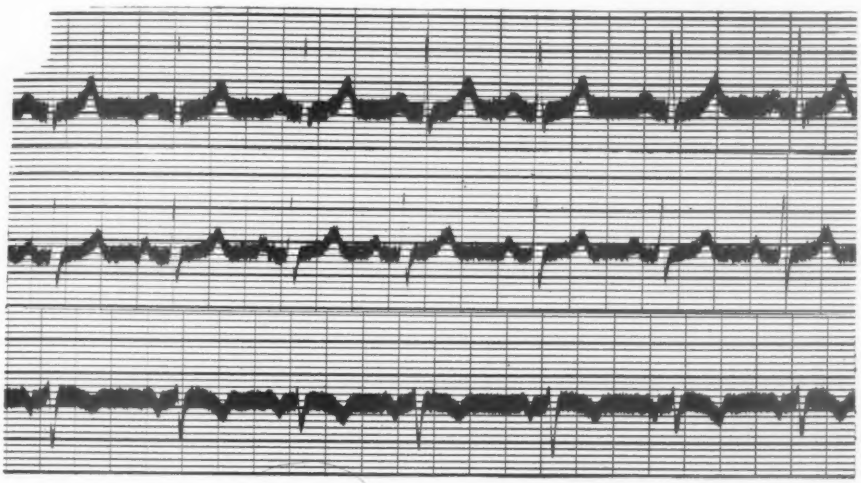

Fig. 1.—An electrocardiogram showing a complete inversion of the P, QRS, and T deflections in Lead III. Note the variation of the QRS amplitude in Lead III with respiration. Lead I corresponds to the usual normal Lead II.

recognized as evidence of congenital dextrocardia (Fig. 2), a condition almost the reverse of that giving rise to inversion of Lead III.

In the Cardiac Laboratory of the Massachusetts General Hospital we have encountered an inverted Lead III 115 times in a review of electrocardiograms of about 8000 patients, an incidence of 1 in 70. Without definite data as to the clinical significance of this finding, it has gradually come to be associated by us with a certain type of individual, most frequently an obese person, or one of a short and "stocky" build. The present investigation was undertaken in order to determine what significance, if any, one could attach to this electrocardiographic finding.

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Inversion of the P-wave alone or associated with other changes in the third lead has attracted the attention of numerous investigators. Einthoven, Fahr, and de Waart[1] pointed out that the P-deflection in Lead III may be considerably modified by the phases of respiration, being lower at the end of inspiration and the beginning of expiration, coinciding with the longer pauses of the cardiac cycle and perhaps depending upon an increase in the vagal tone at that time. However, they caution against attributing these changes entirely to the reflex influence of respiration, and add "that a slight rotation of the heart about the sagittal axis of the body, as is possible with a deep inspiration, is sufficient to modify conspicuously the form and height of the various complexes." Wilson[2] has reported several cases in which the negativity of the P-wave associated with respiration was ascribed to

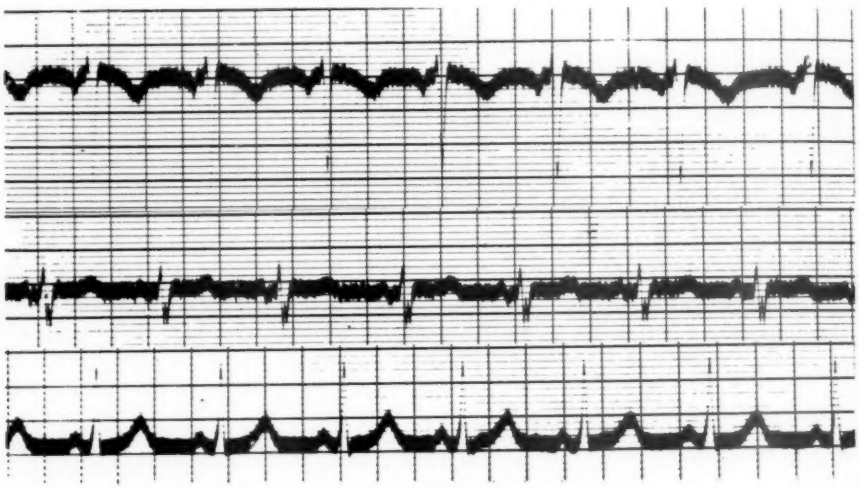

Fig. 2.—An electrocardiogram of a patient with congenital dextrocardia showing an inversion of the P, QRS, and T deflections in Lead I for comparison with Fig. 1. Lead III corresponds to the usual normal Lead II.

a change in the location of the pacemaker; the possible occurrence of a change in the location of the pacemaker had been previously demonstrated by Lewis, Meakins, and White[3] in experimental work on the dog's heart resulting from vagal stimulation. In 1919 Carter and Wedd[4] presented additional evidence showing the effect of the vagi on a change in the location of the pacemaker and an inversion of the P-wave in Lead III. Furthermore, by taking leads from the chest wall Cohn[5] demonstrated not only that the position of the heart in the chest has an influence on the form of the electrocardiogram but also that this influence may be far reaching. By rotating the leads in a clock-wise manner he produced an effect analogous to that which would be caused by rotating the heart to the left and upward, and the resulting electrocardiograms show left axis deviation with inversion

of the P- and T-waves as well as of the QRS waves in Lead III similar in all respects to those encountered in the series which we are now reporting.

In the present study we have collected clinical data on 100 patients whose electrocardiograms showed an inversion of all deflections in Lead III. The average age of the group was 47.3 years; 54 were females and 46 were males. The diagnoses were variable and covered a wide range of medical and surgical conditions. Organic heart disease was present in 55 of the patients, a percentage less than that of the incidence of heart disease in the cases routinely electrocardiographed at the Massachusetts General Hospital (which was 82 per cent of the last 100 cases, for example). Such heart disease was, moreover, only infrequently of considerable degree. Evidence of congestive failure, usually slight, was noted in 11 cases, and 15 patients had received digitalis therapy. Hypertension was present in 33 cases. From our data it seems that the presence or absence of organic heart disease is not an important factor in the inversion of Lead III. The amount of left axis deviation was usually of moderate degree; in only 17 of the patients did it exceed $-30°$ by angle, and in only six $-40°$ (Carter, Richter, and Greene[6]).

TABLE I

THE RELATIVE FREQUENCY IN 100 CASES OF FACTORS PREDISPOSING TO A TRANSVERSE POSITION OF THE HEART WITHIN THE CHEST

| | |
|---|---|
| Obesity | 55 |
| Ascites | 2 |
| Enlarged liver | 2 |
| Enlarged spleen | 1 |
| Large fibromyoma (uterus) | 1 |
| Right sided pleural effusion | 1 |
| Scoliosis of spine to right | 1 |
| Chest deformity (bulging of left side) | 1 |
| High diaphragm without obvious cause | 4 |
| Horizontal position of heart (roentgen ray) | 4 |
| Total | 72 |

In Table I is listed the frequency of certain factors, the presence of which predisposed to a rotation of the heart to the left and upward. It is seen from this table that marked obesity was by far the most common condition found (55 patients), and that in 72 patients (72 per cent) a transverse position of the heart was noted as the result of findings which were sufficiently pronounced to attract the attention of the physical examiner or of the roentgenologist in routine examinations, without attention having been previously called to this feature of the case. Of the remaining 28 patients in which there was no obvious cause for a transverse position of the heart, 24 were well developed and nourished, while 4 were thin and of the type in which one would expect a vertical position of the heart in the chest. Of this

latter group there was no evidence of organic heart disease in 3, while the remaining patient had chronic nephritis and hypertension with moderate cardiac enlargement, chiefly in the region of the left ventricle. In the group of 52 patients who had a roentgen examination of the chest, a high diaphragm was reported by the roentgenologist as a well-marked finding in 24 instances, and slight to moderate left ventricular hypertrophy was noted 41 times. Because of the frequent association of factors tending to elevate the diaphragm in this series, it is probable that the left ventricular "hypertrophy" noted by the roentgenologist was more apparent than real in a considerable number of the cases.

It is of further interest that in most of the subjects with total inversion of the electrocardiographic complexes in Lead III, forced respiration may be used as a diagnostic test. The deepest possible inspiration usually decreases markedly and sometimes abolishes completely the inversion of the complexes; deep expiration, on the other hand, increases the inversion in these cases but usually not a marked degree.

A study of the effects that the enlarged uterus in the later months of pregnancy may have upon Lead III would be of considerable interest, and we are planning to follow up this point. Although we have already found an inversion of the third lead in two patients who were pregnant, electrocardiograms taken after delivery showed essentially the same finding. Both of these women were, however, obese and of the type in which a high position of the diaphragm is frequently encountered.

From the present study we have found that our earlier impression was correct, namely, that the electrocardiographic finding of an inverted Lead III in the majority of instances is associated with a transverse position of the heart most frequently encountered in obese persons with a high diaphragm, and that it is otherwise of little clinical significance. Thus it is evident, as is also suggested by the work of Cohn,[5] that the combination of left axis deviation with an inverted P-wave in Lead III indicates a rotation of the heart as a whole to the left, rather than left ventricular enlargement which might be suspected in a case with a like degree of left axis deviation but with an upright P-wave in the third lead.

From a somewhat different point of view Master and Oppenheimer[7] arrived at conclusions in a large measure similar to ours. In a study of 100 obese persons they found in a considerable percentage (78 per cent of 73 cases studied by roentgen ray) an elevation of the diaphragm and a transverse position of the heart due to the presence of abdominal fat. "Electrocardiograms taken in ninety-seven cases showed definite characteristic changes. Fully 87 per cent showed a left ventricular preponderance, which not only is far beyond the number found in ordinary adults, but for the age groups studied, is an

unusually high figure. A change in the P- and T-waves in the third lead was very common; these waves were either flat (iso-electric) or inverted. The changes in the P-waves occurred in 70 per cent and in the T-waves in 87 per cent of the cases. . . . . Repeated electrocardiograms were taken as the patients lost weight. Of fifteen patients whose average loss in weight was 32 pounds (15 kg.), all but two showed a return toward a normal electrocardiogram; that is, a change from inverted or flat to normal P- and T-waves, and a loss or diminution of the left ventricular preponderance."

## SUMMARY AND CONCLUSIONS

The results of a clinical study of 100 patients with a complete inversion of Lead III of the electrocardiogram are presented. In 72 per cent of the series factors were found on physical or roentgenological examination which predisposed to a transverse position of the heart. Obesity was the most frequent condition encountered (55 per cent of the total series). A completely inverted Lead III in the majority of cases has little clinical significance, other than as an indication of the type of individual; namely, one in which are present conditions giving rise to a high position of the diaphragm and a transverse position of the heart.

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# ACUTE INTERSTITIAL MYOCARDITIS*

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Fiedler[1] in 1899 described four cases of "Acute Interstitial Myocarditis." In each of them the clinical picture was one of rapidly progressive myocardial failure ending in death. At autopsy the only characteristic finding was a diffuse cellular infiltration of the interstitial spaces of the heart muscle. In none of the cases was the etiology of the lesion determined.

Fiedler was not the first to describe this disease, as Steffen,[2] Freund,[3] Rindfleisch,[4] and Wolf[5] had previously reported cases with similar clinical pictures and almost identical pathological findings. However, his name has become associated with this form of heart disease, and it is frequently described in the literature as "Fiedler's Myocarditis." Other terms used are acute, isolated, diffuse, and interstitial. Scott and Saphir[6] have recently reported two cases which belong to this group. They have reviewed the literature on the subject and have found thirty-six cases in addition to their own. Three of these cases we felt should not have been included. One of them is the second case reported by Steffen.[2] In this instance the patient apparently recovered from an infection diagnosed during her life as acute myocarditis and later died of pulmonary tuberculosis. The pathological findings were not given. Another is Baumgartner's case,[7] in which the findings were typical of tuberculosis of the myocardium. The third is the case of Rindfleisch,[4] in which a *Staphylococcus pyogenous citreus* was cultured from the heart and in which the microscopic sections showed multiple pyogenic abscesses of the myocardium.

The variety of the clinical pictures presented by the cases which have been reported leads one to the conclusion that acute interstitial myocarditis is a pathological rather than a clinical entity. This is further borne out by the fact that in no instance has the correct diagnosis been made before death.

In the following case, while the autopsy findings were those of acute myocarditis, the clinical picture resembled closely that of coronary occlusion.

## CASE REPORT

A hospital orderly, aged 39 years, came to the out-patient department of the Presbyterian Hospital on the evening of August 29, 1929, complaining of attacks of pain in the chest occurring at frequent intervals during the previous two weeks and usually brought on by exertion.

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*Family History.*—Noncontributory.

*Personal History.*—The patient was born in Ireland and came to this country when he was twenty-three years old. For the next five years he worked as a painter, but gave up this occupation because of "burning sensations in the stomach" and from that time on worked as a hospital orderly. He was not married. He did not use alcohol but smoked in moderation.

*Past History.*—In 1908, while still in Ireland, he had an operation for varicose veins. Shortly after coming to this country, while working as a painter at St. Luke's Hospital, he had a severe attack of diarrhea which required his spending about three days in the hospital. Fourteen others doing similar work had diarrhea at the same time. He was first admitted to the Presbyterian Hospital in May, 1920, suffering from acute gout. He made a rapid recovery and was discharged after a stay of only three days. Physical examination at that time revealed a heart slightly, if any, enlarged, the cardiac dullness extending eleven centimeters to the left of the midline in the fifth interspace. The sounds were described as being of good quality. The aortic second sound was louder than the pulmonic. No murmurs were heard. The blood pressure was 130/85 mm. The blood Wassermann reaction was negative in both alcoholic and cholesterin antigens. Early in the following year he received treatment for "arthritis of the feet" at the New York Orthopedic Hospital, and in July, 1926, he was treated in the emergency ward of the Presbyterian Hospital for a paronychia of the thumb.

There was no history of rheumatic fever or other previous acute infection. During the first few years of his stay in this country he had frequent colds, but no severe sore throats. Careful inquiry revealed no symptoms referable to the cardiorespiratory system prior to the present illness. He had not had nocturia. There was no story of syphilis or gonorrhea.

*Present Illness.*—For two weeks prior to his last admission the patient had been having fairly frequent attacks of mild pain starting in the region of the sternum, radiating laterally across the upper anterior part of the chest to the right and to the left, to the upper interscapular region on both sides, to both shoulders, and down the inner sides of both arms to the fourth and fifth fingers of both hands. These attacks of pain were associated with a feeling of tightness in the chest. They were quite definitely brought on by exertion and were relieved by rest. They were never very severe and were never associated with any fear. He had had no dyspnea, palpitation, nor edema of the ankles.

*Physical Examination.*—Revealed a rather obese man of 39 years, who did not look at all ill. His complexion was ruddy. His lips showed the very faintest cyanotic tinge. The pupils reacted well to light and during accommodation. The pharynx and tonsils were slightly injected. The lungs were clear, except for signs of moderate emphysema. The heart did not seem to be enlarged, though the obesity and barrel-shaped chest made percussion unsatisfactory. The sounds were distant, but of quite good quality. The aortic second sound was louder than the pulmonic. No murmurs were heard. The blood pressure was 160/100 mm. The radial vessels were moderately thickened. The pulses were equal and of good quality. The rate was not rapid. Examination of the abdomen revealed nothing abnormal.

It was felt at the time that the pain was cardiac in origin, due probably to disease of the coronary arteries. The patient was advised not to report for work that night, to attempt no exertion which seemed to him likely to bring on the pain, and to return to the employee's clinic the next day for a thorough examination.

He did not follow this advice, but worked most of the night. About six o'clock next morning, while in a street car on the way home, he was seized with a very severe pain in his chest, having the same distribution and radiation as those which he had had previously, but accompanied by a frightful sense of constriction under

the sternum and by a fear of impending death. He managed to get back to the hospital by taxi, vomiting once or twice on the way.

When seen in the emergency ward a few minutes later, he was groaning and writhing—apparently in very severe pain—sweating profusely. He said he felt as if his chest were being squeezed in a vise. His skin was cold and moist. His temperature was normal, his pulse not rapid. The heart sounds were much as they had been earlier in the evening, perhaps a little more distant. His blood pressure was 150/120 mm. Nitroglycerine, 0.0006 gm., was given without relief. This was repeated, with similar result. He was then given 0.016 gm. of morphine and moved into a bed in the overnight ward. He seemed to obtain relief from the morphine in a few minutes and fell asleep. An hour later he was still asleep, and his respirations were reported as being regular and of good quality. An hour after this the nurse in charge went to see him and found him dead. Inspection of the

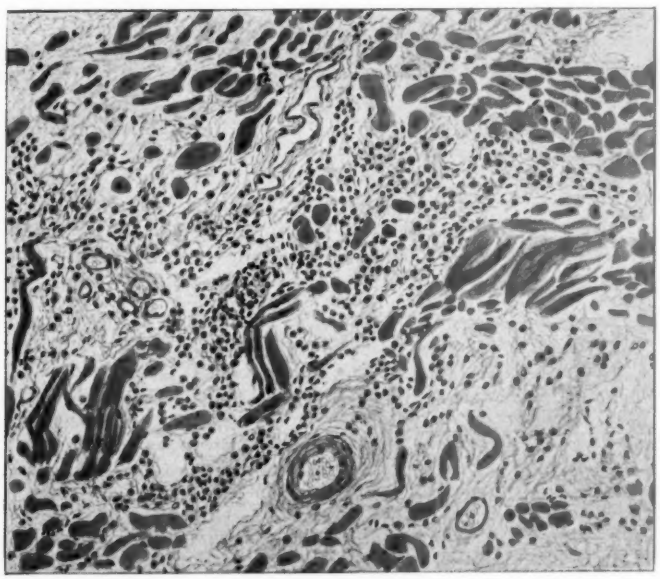

Fig. 1.—Myocardium of the left ventricle. There are some necrotic fibers, but several normal fibers and a normal venule lie in the heavily infiltrated area.

body immediately after death revealed intense cyanosis of the face and mucous membranes. The skin of the body had a dusky hue.

The diagnosis made at the time of death was: General arteriosclerosis, arteriosclerosis of the coronary arteries, thrombosis of the coronary arteries, angina pectoris.

*Pathological Findings.*—The essential pathological findings were the following: The body is that of an obese and muscular white man, 183 cm. in length. The face is red, the fingers and toes are intensely cyanotic. The pupils are equal and in extreme dilatation. The right leg has varicose veins and the scar of an old operation. There is no evidence of a recent wound or infection. The peritoneal cavity contains no free fluid. The peritoneal surfaces are normal. The liver extends 6 cm. below the xyphoid and 3.5 cm. below the costal margin in the right midclavicular line. The other relationships are normal. The right pleural cavity is obliterated by old fibrous adhesions, and a few old adhesions are present in the left pleural cavity. A large persistent thymus lies in its normal position. The pericardial sac contains a normal amount of clear fluid, and its surfaces are smooth and glistening.

*Gross Examination.*—The *Heart* weighs 460 gm. It is extremely flabby in consistency. Both ventricles are hypertrophied and dilated. The epicardium is normal, and there is a moderate amount of subepicardial fat. The right auricle and the tricuspid valve are normal. The right ventricle has thickened walls, measuring 0.7 cm. in thickness near the apex. The conus area is especially dilated, and the wall here measures 0.5 cm. The septum bulges slightly into the right ventricular cavity. The pulmonary valve is normal. The left auricle is normal. The mitral valve shows slight nodular thickening along the margin. Most of the chordae tendineae are normal, but there are several thickened ones which are attached to the posterior leaflet, far from the margin. The columnae carneae are prominent and the papillary muscles well developed. The dilatation of the left ventricle is shown chiefly by the bulging septum. The muscle is soft, very flabby, dark brown and uniform in color, without flecks. The aortic leaflets are soft, but there is some thickening at their attachment. There are several small atheromatous plaques scattered through the coronary arteries. There is no evidence of thrombosis.

*Lungs:* Right, 1080 gm., left, 640 gm. They are heavy, firm, dark purplish red without mottling or nodules. There is an abundance of blood-stained fluid on the

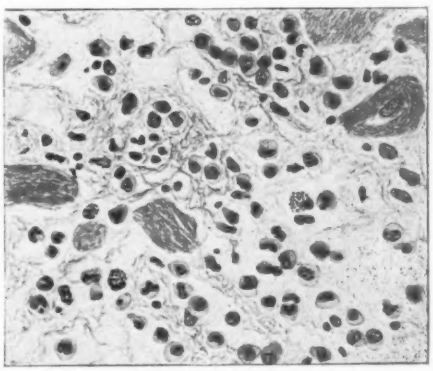

Fig. 2.—High power view of a small area in the infiltrated myocardium of the left ventricle, showing the types of cells present.

cut surface. *Spleen:* 380 grams. It is large and the capsule is tense. On section the bulging pulp is soft and friable, and much excess bloody fluid can be scraped from the surface. *Liver:* 3060 grams. It is firm, with rounded edges and a tense capsule. The cut surface bulges above the capsule, is soft and exudes blood-stained fluid. The branches of the hepatic vein are dilated. *Pancreas:* Normal. *Adrenals:* The left is atrophied, the right has a narrow cortex with a small lipoid deposit. *Kidneys:* Right, weighs 260 grams, contains excess fluid, and is dark red in color. There are a few small hemorrhages in the pelvis. Otherwise normal. *Bladder:* Moderately hypertrophied and dilated. The mucosa is dull red and bears several minute cysts in the trigonum. *Prostate:* Moderately enlarged and contains three firm discrete nodules, each about 5 mm. in diameter, near the urethra. The medium lobe is prominent. *Testes:* Normal. *Stomach:* Normal, aside from several small submucosal hemorrhages. *Intestines:* Normal. *Thymus:* Weighs 40 grams. The lobular structure is preserved, but the outer portion of each lobule appears like a cortex of fat around the pinkish medulla.

*Microscopic Examination.—Heart:* A. Left Ventricle. In the myocardium and but a short distance beneath the endocardium lies a patch of edematous connective tissue infiltrated with many cells. The prominent cell is the polymorphonuclear leucocyte, although there are many eosinophiles and mononuclear phagocytes and oc-

casional lymphocytes and plasma cells scattered among them. In places there are also endothelioid nuclei. The muscle cells in the region are pressed apart. A few fibers are necrotic, but several normal ones traverse the center of the largest infiltrated area. Several small arterioles in the area have thickened walls without a corresponding increase in number of nuclei. This infiltrated area extends to the endocardium in one of the crevices between columnae carneae. The endocardium of the crevice is thickened and occupied by a dense mass of cells of the same types, except for the absence of eosinophiles, to the extent of ten or more cells deep. Throughout the remainder of the section there is a mild increase of cells in the interstitial tissue between muscle fibers, usually consisting of lymphocytes. There are scattered polymorphonuclears in one somewhat more densely infiltrated area. The muscle fibers vary in size, the fibrillae are conspicuous, and the lipochrome content small. The nuclei are normal. The epicardium and superficial fat are normal. No organisms are seen in the gram-stain.

B. Left Ventricle. At the deepest point of the inter-columnar crevices there are endocardial changes which are milder than those in heart A but similar to them.

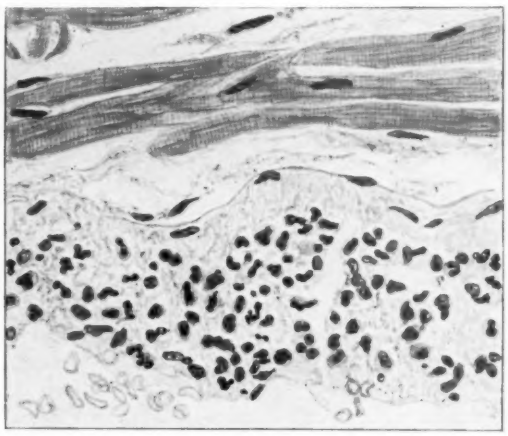

Fig. 3.—Endocardium of the left ventricle. The base of an intercolumnar crypt found in the same section as Fig. 1 and in an adjacent field. The endocardium is densely infiltrated with lymphocytes, mononuclear phagocytes and polymorphonuclear leucocytes.

In one case the cellular infiltration extends up into the muscle for a distance of 0.6 mm. In the diffuse cellular infiltration and the normal muscle fibers this section resembles A.

C. Left Ventricle. There is one area of interstitial infiltration of the same types of cells found in A. There is some interstitial edema.

D. Septum. There is one small cluster of similar cells. The endocardium is slightly thickened but without any increase in the number of nuclei.

E. Right Auricle. Normal.

F. Sino-auricular Node. Normal.

G. Right Ventricle. Normal.

H. Left Auricle. Normal.

I. Mitral Valve. The marginal thickening of the valve consists of homogeneous material with occasional scattered round nuclei. The deeper portion of the section, corresponding to the middle of the valve, has many small blood vessels with scattered round cells about them. There are occasional endothelioid cells near them.

*Other Organs.*—The aorta shows early arteriosclerosis and engorgement of the adventitial vessels, with one small hemorrhage in the adventitia. The spleen is

congested, the Malpighian corpuscles are numerous and small with small hyalinized arterioles. The liver is congested and contains a moderate amount of fat. The adrenals are congested and have a moderate lipoid deposit. The pancreas is congested and contains several small hemorrhages. The kidneys show congestion. The mucosa of the bladder contains many minute cysts in the epithelium of the trigone. There are a few polymorphonuclear leucocytes in the prostatic tubules. Sections from the esophagus, stomach, intestines, and a bronchial lymph node show engorgement of the capillaries and venules. The medulla of the thymus contains a few lymphocytes and Hassall's corpuscles. The cortex is replaced by fat.

*Anatomical Diagnosis.*—Acute myocarditis. Acute endocarditis and valvulitis. Acute passive congestion of the lungs, liver, spleen, kidneys, adrenals, intestines, and lymph glands. Acute prostatitis, adenomata of the prostate. Moderate arteriosclerosis of the aorta. Persistent thymus gland. Fatty liver. Atrophy of the left adrenal. Cystitis cystica. Fibrous pleural adhesions.

## DISCUSSION

In reviewing the clinical history in the light of the post-mortem results one finds little that could give one a clue as to the correct diagnosis. The cardiac pain which the patient had had for two weeks prior to his death was typical of that usually associated with disease of the coronary arteries. The sudden recurrence of this pain with great severity, its failure to respond to nitroglycerine, and the accompanying collapse with weakness, sweating, cyanosis, and sudden death, would lead one to expect that at autopsy one would find sclerosis of the coronary arteries with an occlusion of one of the larger vessels. The only discordant points are that the patient was below the age group in which coronary occlusion is common and that during the terminal attack of pain there was no fall in blood pressure.

Our failure to find anything in the history or physical findings that would have led one before the autopsy to make a correct diagnosis made it seem desirable to review the literature in an attempt to correlate the clinical pictures of the reported cases with the autopsy findings. This was not an easy task, as many of the histories are incompletely given, and in some cases the patients were moribund when first seen, and consequently no histories were obtained.

Table I shows the age incidence in the cases in which the ages were given:

TABLE I

| AGE | NUMBER OF CASES | AGE | NUMBER OF CASES |
|---|---|---|---|
| 1-10 | 3 | 41-50 | 5 |
| 11-20 | 2 | 51-60 | 2 |
| 21-30 | 13 | 61-70 | 1 |
| 31-40 | 4 | 71-80 | 1 |

It is interesting that while the disease may occur at any age, 40 per cent of the patients were in the third decade and 70 per cent were between twenty-one and fifty years of age. The sex was given in 32 cases. Of these 22 were males and 10 females, a ratio of over 2 : 1.

We were especially interested in the occurrence of pain and of sudden death. In no case was there a history of the type of pain usually described as anginal. Pain did occur in ten of the cases in which an attempt was made to give a clinical history. In seven of these it was described as precordial pain or oppression. One had epigastric pain and two had generalized cramp-like abdominal pains. In no case was pain the most striking symptom.

Sudden death without previous cardiac symptoms occurred in three cases. In none of these apparently was death preceded by a typical anginal attack. Gierke's[8] patient, who had apparently previously been perfectly well, suddenly died "while beating the carpet." One of Saltykow's[9] patients died suddenly while he was under treatment for a burn which was healing. One of Zuppinger's[10] patients was being treated for an infection of the groin and suddenly was seized with "cramps" and died. Freund[3] describes a patient who, after having polyarthritis for four months, suddenly went into coma and died. Two of the patients (Lemke's[11] and Schminke's[12]) were in acute heart failure at the time of the first examination, and no previous story was obtained. They died almost immediately. One patient described by Fiebach[13] entered the hospital in acute heart failure and died the next day.

In the other 24 cases in which histories were given, the story was one of progressive myocardial failure. In those in which the down-hill progress was rapid, dyspnea and weakness were the outstanding symptoms, cyanosis and tachycardia the most frequently found signs. In those who ran a longer course, the story was usually one of dyspnea, weakness, and palpitation, with the gradual development of cyanosis, anasarca, and ascites, death usually being preceded by severe congestive failure. Table II shows the approximate durations of these cases.

TABLE II

| DURATION | NUMBER OF CASES | DURATION | NUMBER OF CASES |
|---|---|---|---|
| 1 week or less | 7 | 3 months | 3 |
| "A few days" | 2 | 4 months | 1 |
| 1 to 2 weeks | 4 | 8 months | 1 |
| 2 to 3 weeks | 1 | 9 months | 1 |
| 5 to 6 weeks | 1 | 1 year | 1 |
| 2 to 3 months | 1 | 21 months | 1 |

In none of the cases did examination of the heart during life give any clue as to the type of lesion present. In practically all, the heart was enlarged. The sounds were usually described as being of poor quality. None had murmurs suggesting endocardial lesions. In most of them the pulse was weak and rapid. Of the 23 cases in which the temperature was mentioned 17 had fever and 7 had normal or subnormal temperature.

The etiology of the disease has not been determined. Histories suggestive of rheumatic fever were obtained in only three cases. One of the patients reported by Scott and Saphir[6] had had rheumatism twenty years before and a mild cardiac break ten years before. Stolz's[14] patient had had polyarthritis one year before. In only one case, Fiebach's,[13] was there a history of previous syphilitic infection.

However, in reviewing the reported cases one is impressed by the number in which symptoms of decompensation started suddenly during or shortly after an acute infection. Kaufmann,[15] in discussing this point, suggests that the myocardial lesions may be the result of the toxic action of bacterial products. In support of this hypothesis he mentions two cases of his own, of which one had an infected burn and the other an infection of the operative wound following the removal of tuberculous cervical lymph nodes. One of Saltykow's[9] patients had a healing burn; the other had had an incision for drainage of an abscess of the jaw ten days before the onset of symptoms of heart failure. One of Sellentin's[16] patients had had a carbuncle of the neck opened four weeks previously. Wolf's[5] patient had a traumatic abrasion of the arm. Zuppinger[10] reports a case in which an infection of the foot was incised thirteen days before the onset of cardiac symptoms. His other patient had a skin infection of the left groin. One of Fiedler's[1] patients had been troubled for some time with leg ulcers, and another had previously had a hemorrhagic skin eruption. In most of these cases death came suddenly or after a very short and rapidly progressive illness. "Grippe" preceded the onset of cardiac symptoms in Hafner's[17] case and in one of the cases reported by Scott and Saphir.[6] Fiebach[13] reports a patient whose illness started with a cold and high fever. Bilateral otitis media (Pfeiffer bacillus) developed, soon to be followed by symptoms of decompensation. Death occurred eight days after the onset. Pal's[18] patient had had acute gonorrheal urethritis two months before the onset.

While there is no proof that these infections were the causative factors in the production of the myocarditis, one cannot avoid being impressed by the large number of cases in which they preceded very closely the onset of myocardial failure.

A fairly full pathological study has been reported in thirty of the cases in the literature. These cases are those of Freund,[3] Wolf,[5] Fiedler[1] four cases), Josserand and Gallavardin[19] (three cases), Zuppinger[10] (two cases), Sellentin[16] (two cases), Saltykow[9] (two cases), Cohn,[20] Pal,[18] Fiebach[13] (two cases), Gierke,[8] Shilling[21] (two cases), Schminke,[12] Hafner,[17] Stoltz,[14] Lemke[11] (first case), Mordre,[22] Scott and Saphir[6] (two cases), and our own case.

The one constant pathological finding is the presence of changes in the myocardium, and these changes are consistently the same only in the microscopic sections. In every case there are also gross changes in

the heart. In the majority of cases the heart is hypertrophied to a moderate degree, although in the two cases reported by Scott and Saphir,[6] and in Wolf's Case 5 the heart weighed over 600 grams. In three of the five cases without hypertrophy death occurred within a few days after onset, and in the other two the interval is not stated. On the other hand, in thirteen of the patients who died less than two weeks after the first onset of symptoms, and in several of the cases of sudden death, there was definite hypertrophy, indicating a process of much longer duration than the symptoms. The hypertrophy is always of the left ventricle and sometimes also of the right. There is dilatation of the ventricles in most of the cases. Usually the left ventricle is dilated, and in many cases both are affected equally.

The most prominent lesion is always in the myocardium. When the consistency of the muscle is mentioned, it is usually said to be extremely flabby (nine cases), as in the present case, although in other instances (five cases) it is firm. An attempt to correlate this point with the duration of the disease shows that the flabby myocardium is more often associated with a brief course and the firm one with a more prolonged illness, but that there are exceptions in both case groups. In twenty-three of the thirty cases the myocardium is described as mottled with greyish-yellow streaks and flecks which show through the endocardium but appear most clearly on the cut surface of the muscle. The left ventricle and sometimes the right are involved, although the auricles sometimes have the same appearance. The muscle between these pale spots is usually very dark red. This description is so consistently met with that it is surprising to find five cases, including the one here reported, in which there was no gross abnormality in the color of the heart muscle. In four cases it is a homogeneous dark red, and in the fifth it is described as greyish-red. The presence of mural thrombi in ten cases is also not surprising. The thrombi are most often in the apex of the left ventricle; in two cases they are in the apex of the right ventricle; in one case, in both ventricles, and in two cases in the left auricle. In eight cases the expected widespread infarction of the viscera is found. The presence of thrombi can be correlated with the duration of the disease. Mural thrombi were present in eight of the ten cases with symptoms extending over one month or more. Mural thrombi were also present in Shilling's case[21] of fourteen days' duration and in Fiebach's case[13] of one day's duration. The case here presented shows acute endocarditis involving the crevices between the columnae carneae (Fig. 3), and it is easy to conceive of thrombus formation on such a surface.

In four of the cases there was nodular thickening of the mitral valve, and in one there was thrombosis of the anterior descending branch of the left coronary artery, with beginning infarction of the area supplied by it. There were no other complicating heart lesions.

The microscopic picture of the myocardium is singularly uniform. There is an infiltration of many cells with lymphocytes and mononuclear phagocytes as the most numerous cell types, and with eosinophiles, polymorphonuclear leucocytes and fibroblasts in lesser numbers. These cells are found in clumps or scattered among the muscle fibers singly, or they lie in the perivascular connective tissue. Many minor changes in the muscle fibers have been reported, but these appear to be secondary in importance. There are a few necrotic fibers in and around the foci of invading cells, and sometimes multinucleated fragments of muscle cells. In several cases of longer standing (Josserand and Gallavardin[19]), there is much scar tissue. In every case three points are noted: (1) the lymphocytes and the mononuclear phagocytes are the prominent cells; (2) the infiltration is primarily in the interstitial tissue; (3) neither cultures nor specially stained slides have ever revealed any bacteria or spirochetes, with the single exception of Rindfleisch's case[4] which we have ruled out of our discussion.

The other organs show acute passive congestion in 19 cases. Occasionally only the lungs show it. There are also many infarcts in the cases having mural thrombi. In several cases foci of infection were revealed, in addition to the cases where infection could be noted clinically. They are: The case of Josserand and Gallavardin[19] in which there was tuberculosis of the axillary lymph nodes; Freund's case,[3] in which a macerated Tænia solium was recovered from the intestine and cysticerci were found on the cerebral cortex; Fiebach's first case[13] in which there were chronic nephritis and cholelithiasis: his second case in which there were abscesses in the right ear and an aortic lesion which was probably luetic; Gierke's case,[8] in which the tonsils exuded pus and the pelvis contained a chronic infection; and Saltykow's case, in which were found caseous pulmonary tuberculosis and parenchymatous degeneration of the kidneys. In general, there were no frequently repeated lesions other than these in the heart, and the congestion and infarction subsequent to them; but there were pyogenic infections sometime in the course of eleven out of the thirty-two cases reported; something resembling grippe associated with the onset in three, and specific infections such as tuberculosis or gonorrhea in five.

## SUMMARY

A case is reported in which the clinical picture simulated that seen in coronary occlusion, but the pathological findings were those of acute interstitial myocarditis. In a brief review of the literature the following points stand out:

1. The diagnosis is necessarily a pathological one, since there is no uniform clinical picture.

2. While sudden death sometimes occurs, in the majority of cases death is preceded by symptoms of progressive myocardial failure of variable duration.

3. Although there is no known etiology, the frequent association with infections, especially pyogenic infections of the skin, is suggestive.

4. Analysis of the pathological findings in thirty cases reveals the fact that the microscopic picture is the one constant finding.

5. In the majority of the cases there are also cardiac hypertrophy and dilatation, a greyish-yellow mottling of the myocardium of the left or both ventricles, and acute congestion of the viscera.

6. In most of the cases of more than one month's duration there are mural thrombi in the left ventricle.

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# CALCAREOUS AORTIC VALVULAR DISEASE*

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THE etiology of a markedly calcareous, frequently stenotic valvular lesion confined almost entirely to the leaflets of the aortic valve is puzzling to the pathologist. Occasionally this lesion is so striking, in contrast with total lack of any other signs of disease of the cardiovascular system, that the etiological factor seems hopelessly concealed. From the clinical standpoint, too, this condition sometimes presents incongruities. There may be marked incompetence of the valve, considerable stenosis, and evidence of valvular disease of long duration, but absence of symptoms of cardiac disease. Not infrequently the lesion found at post-mortem examination has been entirely unsuspected. The lack of clinical awareness of the existence of this condition can be accounted for, in large measure, by the scanty attention that the subject has received in the medical literature of recent years.

A study of the clinical course of this disease and of its pathogenesis, and an attempt to elucidate its etiology seemed indicated. Therefore thorough clinical and pathological investigations of the condition were undertaken.

In view of the fact that the lesion of the aortic valve in such cases is probably one of long standing, it appeared that evidence of its pathogenesis may have been hidden by the extensive calcification which occurs. Hence, it seemed necesary to construct a conception of the probable pathological process by thorough analysis of the clinical data as well as by pathological studies. This was attempted by means of a review of the clinical and pathological records and by gross and histopathological studies of the heart, including histological studies of the myocardium, of the aortic valves and occasionally of the mitral valves, and of the arch of the aorta.

## REVIEW OF LITERATURE

From a view of the clinical data and the pathological specimens of twenty-eight cases of "pure aortic disease," Cabot[2] concluded that these cases of solitary aortic stenosis are related etiologically to rheumatic endocarditis. This conclusion was arrived at despite certain important facts which the author admitted militated against this hypothesis. Cabot pointed out that in his series of twenty-eight cases of pure aortic disease, only three occurred in females and twenty-five in

*From The Mayo Clinic.

males. The age incidence of these lesions was also strikingly different from that encountered in apparently proved cases of rheumatic carditis, for only six patients of this series were less than forty years old and half the patients were more than fifty years old when they were first seen. "Such an incidence as regards age and sex," stated Cabot, "contrasting strongly as it does with that of the recognized rheumatic cases, cannot help making us suspect at once that these cases belong to a separate group, and are very possibly of a different etiology." Yet in this series of cases a history of rheumatic fever, chorea, or tonsillitis was about as frequent as in the group of cases designated rheumatic.

Cabot could not find evidence of syphilis as a cause of the lesion. Neither could he find unequivocal evidence for an arteriosclerotic basis of the affection. He was impressed by the similarity of the pathological pictures in the valves in the cases of pure aortic stenosis and in those of juvenile rheumatic endocarditis and laid great stress on the occurrence of acute aortic endocarditis in several cases of pure aortic disease, assuming that the acute process is a recrudescence or relapse on the basis of a healed process of like type. What appeared to militate most strongly against the general hypothesis of arteriosclerosis for the whole group is the absence of arteriosclerosis in other parts of the circulatory system in twelve cases of the series.

In a study of the various types of valvular diseases of the heart, Clawson, Bell and Hartzell[3] found fifteen hearts in which there was marked thickening and stiffening of the leaflets due to large calcareous nodules within them. The position of these nodules in no way corresponded to that of the vegetations of active endocarditis, although varying degrees of calcification were found to occur in valves which gave evidence of subacute bacterial endocarditis. The average age of the patients with aortic nodules was fifty-four and a half years. These investigators could not find satisfactory evidence in favor of inflammatory origin of these calcareous lesions in the fifteen hearts in which there was evidence of predominant calcareous aortic valvular disease. They asserted the belief that the calcified nodular type of old valvular defect may originate entirely independent of an inflammatory process, and concluded that the etiology of this type is unknown.

Mönckeberg[8] concluded that calcification of the aortic valves is not the result of an inflammatory process, but rather the result of a degenerative process with secondary deposition of calcium.

Commenting on the possible mechanism of development of nonbacterial, chronic cardiovalvular disease, Thalhimer[10] wrote: "Some general toxic or some distant infectious process might result in a primary trauma to a heart valve. . . . . Thickening of the valve follows, and these thickened valves have been found to be free from bacteria. Thus, the process of valve thickening can be regarded as nonbacterial

in origin. . . . . This may eventually produce a marked stenosis with a shelf-like formation at the line of valve closure." He then added: "Fibrosed, thickened and stenosed valves, found in general arteriosclerosis can be explained similarly. The unusual amount of calcareous deposit in these cases is undoubtedly part of the process of arteriosclerosis, probably initiating the valvular lesion and undoubtedly contributing markedly to its progression."

## MATERIAL FOR STUDY

Altogether forty-two cases of calcareous endocarditis of the aortic valve were available for study. This represents a consecutive series of cases as they came to necropsy between the years 1922 and 1930, except for several cases in which the hearts were not available for study. These cases were selected on the basis of the existence, pathologically, of calcareous infiltration of the leaflets of the aortic valve, in the absence of significant degrees of involvement of other valves. Not infrequently, however, very small atheromatous plaques occurred within some of the leaflets of the mitral valve, or slight thickening of the leaflets of the mitral valve was observed. However, such pathological changes as occurred in the leaflets of the mitral valve may be disregarded in our present consideration, since such changes, in general, occurred not more frequently nor to any greater degree than may be observed in apparently normal hearts of persons of the ages corresponding to those of the patients in our series.

## ANALYSIS OF CLINICAL DATA

It is significant that a history of "rheumatism" was elicited in only three cases, and in one other case recurrent attacks of chronic arthritis and myositis had occurred for a period of ten years. Tonsillitis occurred in five cases, influenza in thirteen cases, and scarlet fever in eight cases. In one case, in which there was a history of syphilitic infection eighteen years previously, there was no clinical evidence of this infection, and the Wassermann reaction of the blood was negative. In another case, the Wassermann reaction of the blood was strongly positive, but neither a history of the primary syphilitic lesion, nor signs of syphilis, could be elicited. In two other cases there was a history suggestive of syphilitic infection, of which definite confirmatory evidence was lacking.

*Distribution by Sex and Age.*—In the forty-two cases there were eight females and thirty-four males. With the exception of one patient, who was twenty-five years old, the ages of the patients when first seen at the clinic varied from thirty to eighty-seven years. As can be seen in Table I, only three patients were less than forty years old, and thirty-five patients were more than fifty years old when they presented themselves for the first examination. Seven patients were

examined at the clinic on more than one occasion, at intervals varying from four to eighteen years. Although the presenting complaint at the first examination in six of these cases was not referable to the heart, a record of the occurrence of persistent cardiac murmurs at the first examination in each instance, and subsequent finding of the valvular lesion indicate the probable existence of the cardiac lesion at the time of the first examination. One of these patients came primarily on account of indefinite precordial distress. This patient lived for eleven years thereafter and died of cardiac decompensation and paroxysmal tachycardia. One other patient, who was first seen at the

TABLE I

AGE AND SEX INCIDENCE

| AGE, YEARS | MALE | FEMALE |
|---|---|---|
| 25 | | 1 |
| 30 to 39 | 2 | |
| 40 to 49 | 3 | 1 |
| 50 to 59 | 6 | 3 |
| 60 to 69 | 11 | 3 |
| 70 to 79 | 8 | |
| 80 to 89 | 4 | |
| Total | 34 | 8 |

age of thirty years, on account of chronic arthritis, died suddenly ten years later, in an attack of cardiac decompensation. In the remaining five cases of this group death was primarily ascribed to conditions other than cardiac, and during life there were few symptoms attributable to the cardiac defect.

## SYMPTOMS AND SIGNS

The most striking feature with regard to symptoms in this group of cases is lack of any characteristic complaints. Often symptoms referable to the cardiovascular system are not present. As may be seen in Table II, only six patients presented themselves for examination primarily on account of symptoms which were attributed directly to the heart. Two other patients complained of symptoms typical of angina pectoris, associated in one instance with frank hyperthyroidism and in the other with pernicious anemia. Haines and Kepler[4] have pointed out the part played by hyperthyroidism in precipitating the syndrome of angina pectoris, and Willius and Giffin[13] have observed a similar effect of pernicious anemia in certain cases. Both of these patients, however, were found to have considerable sclerosis of the coronary arteries, making it more likely that the anginal pain was due directly to this cause. In one instance, in which disease in the aortic valve was found at necrospy, the patient had not been under observation of physicians at the clinic and a detailed history was not available. When cardiac symptoms were noted by the patient, in general they ranged

from a complaint of slight dyspnea on exertion indicative of myocardial insufficiency, to symptoms resulting from a severe grade of cardiac decompensation.

As might be expected, dyspnea was the most common of the cardiovascular symptoms and was noted in twenty-one cases. Eight patients complained of palpitation; this symptom could be attributed to an associated condition, such as hyperthyroidism in several instances.

TABLE II

PRIMARY CONDITIONS FOR WHICH PATIENTS PRESENTED THEMSELVES FOR EXAMINATION

| CONDITION | CASES |
|---|---|
| Myocardial decompensation | 4 |
| Myocardial decompensation and coronary sclerosis | 2 |
| Hypertrophy of prostate gland | 6 |
| Hyperthyroidism | 4 |
| Carcinoma of rectum | 4 |
| Carcinoma of bladder | 3 |
| Carcinoma of prostate gland | 1 |
| Carcinoma of esophagus | 1 |
| Carcinoma of thyroid gland | 1 |
| Carcinoma of breast | 1 |
| Exophthalmic goiter and angina pectoris | 1 |
| Empyema of gall bladder | 1 |
| Pernicious anemia and angina pectoris | 1 |
| Intestinal obstruction | 1 |
| Erysipelas | 1 |
| Tumor of brain | 3 |
| Cerebral arteriosclerosis | 1 |
| Cholecystitis with stones | 1 |
| Myeloma of sternum | 1 |
| Vesical calculus | 1 |
| Pneumonia | 1 |
| Epigastric hernia | 1 |
| No history | 1 |

Otherwise, patients who presented evidence of myocardial insufficiency had palpitation. Eight patients complained of weakness, but the majority of these had some concomitant condition which seemed to account for the complaint. Others had it in the presence of cardiac failure. Seven patients complained of slight cough, and two had had vertigo.

Four of the forty-two patients had precordial pain. Two of these had pain typical of angina pectoris; it was precipitated by exertion and radiated to the left arm. Two other patients complained of substernal oppression or indefinite precordial pain on exertion.

On general examination the patients usually were found to be fairly well nourished. There was not any particular tendency to obesity. When there was evidence of considerable loss of weight, this could be ascribed to some condition other than the cardiac defect.

Pallor was observed in three cases. In at least two of these it was not related to the cardiac condition. Cyanosis, which was observed in four cases, always was associated with a marked degree of cardiac

decompensation. Varying degrees of passive congestion were observed in thirteen cases. Usually this was manifest by only slight pitting edema of the ankles or by the presence of numerous moist râles at the bases of the lungs. Rarely massive edema occurred, and that always in association with other signs of marked decompensation.

Varying degrees of cardiac enlargement were noted clinically in twenty of the forty-two cases. In one case, the measurements of the area of cardiac dullness were within normal limits. Records of the size of the heart in the remaining cases were not available. The pulse rate ranged from 64 to 190 beats a minute. The highest pulse rate occurred in a case of paroxysmal tachycardia. Usually the pulse rate was within normal limits. When tachycardia existed, it usually was in a case in which some associated condition was present, such as hyperthyroidism, or some infectious process outside of the cardiovascular system. In several cases the tachycardia was associated with cardiac decompensation.

Auricular fibrillation occurred in seven cases. In three of these, frank hyperthyroidism existed. Premature contractions were observed in three cases. In the remainder, the pulse was of normal rhythm.

In twelve of the cases the systolic blood pressure recorded at the first examination ranged above 160 mm. of mercury. The highest readings recorded in two cases were 220 systolic and 70 diastolic, and 210 systolic and 98 diastolic. The presence of a Corrigan pulse was not noted in either of these two cases. Some of the cases in which relatively low readings of blood pressure were found presented evidence of myocardial insufficiency. In several cases the blood pressure, several months or several years prior to the last examination, revealed evidence of moderate hypertension, whereas at the time of the last examination the readings of blood pressure were distinctly lower. There was no clinical or pathological evidence of myocardial infarction in any of these cases, and the decline of the blood pressure was not necessarily associated with evidence of significant degrees of myocardial insufficiency.

In twenty-two of the forty-two cases there was clinical evidence of sclerosis of the palpable peripheral arteries. In the other cases, specific mention of the condition of the arteries was not made. Of the twenty-two cases of peripheral arteriosclerosis, the degree of sclerosis was graded slight in ten cases, moderate in five cases, and marked in two cases. The degree of sclerosis in the other five cases was not recorded.

It is remarkable how variable were the physical manifestations in the heart and how markedly the physical signs in these cases differed from those regarded as diagnostic of aortic stenosis or insufficiency. The cardiac murmurs varied both in situation and in character. In

nine cases, the murmur was heard over the entire precordium and was usually systolic, and loud or squeaking in character. In one of these cases both a presystolic and a systolic murmur were heard over the entire precordium. In six cases a loud or rough systolic apical murmur only was heard. This murmur was usually transmitted to the axilla only, or to the axilla and over the precordium. In seven other cases, systolic murmurs were heard over both the aortic and mitral areas. In two of these cases the murmurs were described as being musical; in one case the murmurs were soft and blowing. In three cases a roughened systolic murmur, varying greatly in intensity, was heard with maximal intensity over the aortic area and was transmitted upward to the vessels of the neck. The presence of a thrill was not recorded in any of these three cases. In one case a loud, diastolic murmur, heard best over the aortic area and transmitted down the sternum, was associated with a soft, blowing systolic, apical murmur. In another case, a rough systolic and a faint diastolic murmur were heard over the aortic area, associated with a systolic apical murmur. In still another case, to-and-fro aortic and apical murmurs were heard. Murmurs occurring in two other cases were insufficiently described. In twelve cases there was no record of a murmur having been heard.

In two cases in which the occurrence of a thrill was mentioned, it was felt over the region of the apex.

The second aortic sound was recorded as being absent in one case, and paradoxically, accentuation of the aortic second sound was heard in three cases. In one of these there was stenosis of the aortic valve due to a marked degree of calcification of the leaflets. In the two other cases, the degree of calcification was relatively slight.

Electrocardiographic records were available in seventeen cases. In general, significant abnormalities in the electrocardiogram were comparatively uncommon. Inversion of the T-wave in Lead I alone occurred in three cases; in Leads I and II in one case; in Leads II and III in one case, and in Lead III alone in three cases. Left ventricular preponderance was noted in nine cases, and right ventricular preponderance in four cases. Auricular flutter and ventricular premature contractions were noted in one case. Incomplete bundle-branch block with prolongation of the QRS interval to 0.13 second was observed in one case. Notching of the QRS complex in isolated or multiple derivations was noted in several instances.

Roentgenograms of the thorax were available in twenty-eight cases and usually confirmed the clinical impressions regarding the increase in the size of the heart. In three cases the roentgenogram revealed regions of calcification in the arch of the aorta. Marked torsion of the arch of the aorta was reported in two cases, and dilatation of the arch of the aorta in two cases.

Records of examinations of the ocular fundi were available in fifteen cases. Sclerosis of the retinal arteries, of mild or moderate degree, was observed in four cases. In one case the fundus revealed only mild retinal arteriosclerosis of the senile type. In two cases, in which there was evidence of tumor of the brain, the fundus revealed choked disks. In the remaining eight cases the fundi were essentially normal.

Other indications of arteriosclerosis were the occasional presence of clinical evidence of cerebral arteriosclerosis, or roentgenologic evidence of calcification in the peripheral arteries in the legs.

A clinical diagnosis of cardiovalvular disease was made in only seven cases. Among these, aortic stenosis was diagnosed in only two cases. This was suspected clinically as being on an arteriosclerotic basis. The clinical diagnosis in these seven cases was as follows: aortic sclerosis and mitral regurgitation(?); mitral regurgitation; chronic mitral endocarditis with stenosis (one year later in the same case a diagnosis was made of coronary and aortic sclerosis with paroxysmal tachycardia and congestive failure); probably aortic regurgitation, the diagnosis being changed ten years later to rheumatic mitral stenosis and insufficiency; aortic stenosis; aortic stenosis and insufficiency and mitral insufficiency, and suspicion of mitral insufficiency. A diagnosis of aortic sclerosis was made in two cases. In the other cases, the existence of valvular disease was not suspected.

A review of the primary causes of death in these cases also brings out rather surprising facts. Although the pathological appearance of the cardiac lesion gives evidence of long duration of the process, death that could be ascribed primarily to the cardiac lesion was infrequent. Table III shows that in only ten cases was death due to cardiac decompensation, and in one of these cases the cardiac decompensation was associated with generalized sepsis. In five other cases death occurred suddenly. In three of these cases considerable sclerosis of the coronary arteries was found, without evidence of occlusion, however; in

TABLE III

MODE OR PRIMARY CAUSE OF DEATH

| CAUSE OF DEATH | CASES |
|---|---|
| Myocardial decompensation | 9 |
| Myocardial decompensation with sepsis | 1 |
| Sudden death | 5 |
| Uremia and pyelonephritis | 9 |
| Pneumonia | 5 |
| Pulmonary embolism | 2 |
| Emaciation | 2 |
| Postoperative shock | 2 |
| Gastric ulcer and hemorrhage | 1 |
| Edema of glottis | 1 |
| Peritonitis | 1 |
| Respiratory failure (cerebral tumor and fracture of cervical spine) | 2 |
| Mesenteric thrombosis | 1 |
| Carcinoma of pancreas | 1 |

one case there was severe cardiac decompensation. The fifth case in which sudden death occurred was that of a woman, suffering from exophthalmic goiter associated with auricular fibrillation and congestive cardiac failure. At necropsy the coronary arteries were found not to be sclerosed, but there was stenosis of the aortic valve due to fusion and calcification of the right and left anterior aortic cusps. Death in the remaining cases of our series was due to various causes not directly attributable to the heart.

### ANALYSIS OF PATHOLOGICAL DATA

*Weight of the Heart.*—As may be noted in Table IV, the weights of the hearts varied markedly. In some cases the heart weighed less than 300 gm. whereas in others it exceeded 500 gm. In one case, the heart weighed 740 gm. It is difficult to determine with accuracy the factors that played the greatest part in causing the degree of cardiac hypertrophy. Excluding such factors as the variations in body weight and in the age of the patients, factors which could not by themselves effect such wide variations in the size of heart, we have left several other factors which must be considered. Marked variations in the blood pressure, although not a striking feature when the patients were seen at the clinic, might have played an important part in previous years. Undoubtedly the presence of insufficiency, stenosis, or of both insufficiency and stenosis of the aortic valve was responsible in most cases for the marked ventricular hypertrophy, but the existence of valvular insufficiency or stenosis was not always apparent at necropsy when it probably existed during life. It seems most probable that a combination of various factors is the cause of the variable degree of hypertrophy which occurs in these hearts.

*Pericardium.*—One case of typical calcareous aortic valvular disease was associated with adhesive pericarditis which had entirely obliterated the pericardial sac. Evidence of pericarditis was not seen in the other hearts of the series. In seventeen cases the pericardial cavity contained an excess of clear, straw-colored fluid which ranged in

TABLE IV

WEIGHTS OF HEARTS IN GRAMS

| 200 TO 299 | 300 TO 399 | 400 TO 499 | 500 TO 599 | 600 TO 699 | 700 TO 799 |
|---|---|---|---|---|---|
| 265 | 308 | 428 | 550 | 675 | 740 |
| 283 | 328 | 420 | 500 | 685 | |
| 205 | 370 | 480 | 500 | | |
| 230 | 365 | 435 | 543 | | |
| 275 | 360 | 450 | 530 | | |
| | 384 | 402 | 504 | | |
| | 380 | 443 | 565 | | |
| | 367 | 410 | 514 | | |
| | 370 | 442 | 509 | | |
| | 313 | 483 | 595 | | |
| | 322 | 415 | | | |
| | 300 | 410 | | | |

amount from 20 to 200 c.c. In twenty-one cases there was no excess fluid, and in four cases the quantity of pericardial fluid was not recorded.

*Cardiac Valves.*—In the mitral, tricuspid and pulmonary valves there were no significant pathological features. We have already referred to the slight atheromatous changes observed occasionally in the mitral valve.

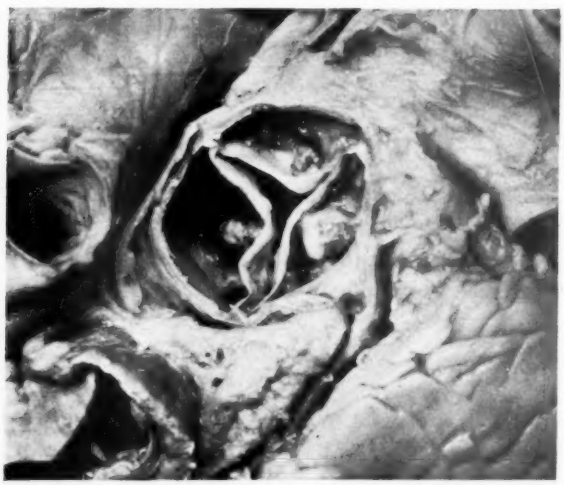

**Fig. 1.—Superior surface of aortic valve. Irregular nodular infiltration with calcareous material, producing distortion of valve and stenosis (natural size) is shown.**

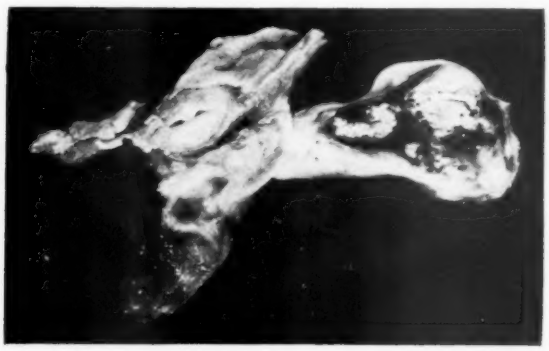

**Fig. 2.—Cross-section of aortic valve leaflet. Marked calcareous deposition within the valve leaflet is shown, the calcareous nodule being covered by endothelium.**

Only the aortic valve presented the significant and solitary valvular defect, which was characterized in general by a variable amount of calcareous deposition within the valve leaflets producing distortion and stiffening of the valves and, in certain instances, varying degrees of stenosis, insufficiency, or both. A characteristic feature of the process was the involvement primarily of the aortic ring, frequently of one of the commissures, and, in more markedly involved valves, ex-

tension of the pathological process onto the valve leaflets (Fig. 1). Rarely did the calcified deposits extend quite to the free margin of the valve leaflets, unless the process was extremely marked. The areas of calcification appeared as whitish, or grayish-white nodules, each with an irregular outline and surface, although at times the surface was smooth. In the milder degrees of involvement, palpation of the aortic

Fig. 3.—Fusion of the right and left anterior cusps of the aortic valve by infiltration with calcareous material.

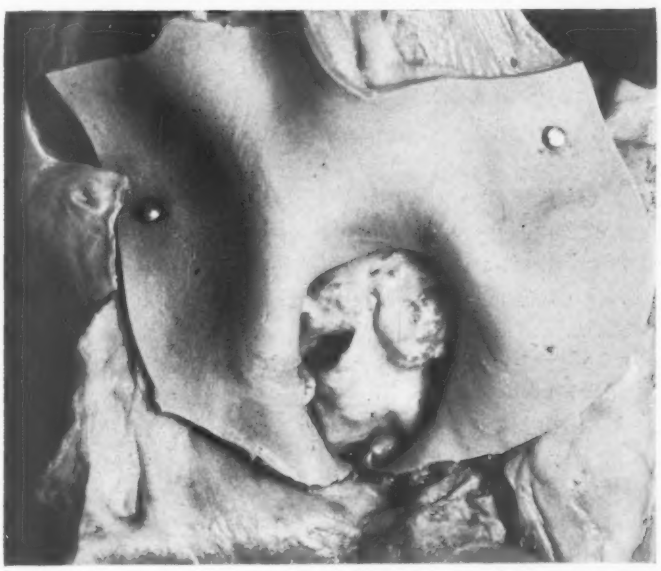

Fig. 4.—Marked degree of calcareous infiltration in aortic valve, producing fusion of all cusps and marked stenosis.

margin revealed a firm, irregular, calcareous ring with spicules of calcium projecting onto the aortic surface of the attached border of the valve leaflets. Several small, calcified nodules might also be felt scattered on the aortic surface of the cusps nearer the ring than the free margin. These nodules appeared to be completely covered by endothelium, which, except for its irregular contour, contained noth-

ing of note (Fig. 2). Frequently fusion of the edges of the cusps was found. In twenty of the forty-two hearts examined, this fusion involved the adjacent edges of the right and left anterior cusps (Fig. 3). In five of these cases, fusion of the cusps was not complete, the process extending from the commissure for a distance of a third or a half of the width of the edge of the cusp. At times this fusion was due only to fibrous tissue, but usually there was found deposition of a variable amount of calcium, which, when abundant, seemed to creep into the adjacent portions of the cusps and to extend beneath the endothelial points on the aortic surface of the cusps. The remainder of the valve might appear entirely normal, or a variable degree of thickening and stiffening might be present. In five hearts, the deposition of calcium occurred between the edges of the right anterior and the posterior cusps, producing partial or complete fusion between them. In two cases in which the process of calcification was extensive, all cusps were fused and were infiltrated with large amounts of calcium, thus forming a rigid diaphragm in which there was a small irregular opening through which the blood entered the aorta (Fig. 4).

The gross appearance of the valves with the less extensive degree of calcification revealed the process to be confined to the subendothelial layers of the valve. The calcium was irregularly distributed, and the process must have begun nearer the aortic than the ventricular surface of the valve, for in earlier stages, when the masses of calcium were still very small, they projected onto the aortic surface of the valve rather than onto the ventricular aspect. The inferior surface of the valve was, in fact, perfectly smooth and regular, whereas the aortic aspect presented an irregularly nodular appearance. The endothelium appeared to be intact, and no vegetations or thrombi were to be found.

In the more severe grades of involvement the nodules of calcium were larger and more numerous, and were spread irregularly on the surface of the aortic valve. When the extent of the process was marked, nodules of calcium might also appear on the ventricular surface of the valve. Even with fairly extensive infiltration of the cusps with calcium it might, however, often be seen that the process still remained confined to the subendothelial tissue. However, not infrequently, there was ulceration of the surface endothelium over the most prominent nodular areas of such valves. The areas between the nodules might appear normal or might be somewhat thickened.

Occasionally the infiltration with calcium extended from the aortic ring onto the immediately adjacent portions of the aorta. The process was never observed to extend far enough onto the aorta to involve the orifices of the coronary arteries.

The degree of stenosis or insufficiency which resulted from this process in the aortic valve could not always be estimated from the examination of the pathological specimen. In at least twenty-two

hearts the stiffening of the leaflets of the valves was such as to make it appear that a variable degree of stenosis must have existed, and in at least seven hearts the extensive stiffening and calcification of the valves undoubtedly produced both stenosis and insufficiency. How often insufficiency alone existed, it was more difficult to estimate. When all three cusps were involved, and were transformed into a rigid diaphragm, the valvular opening might be extremely small, measuring in some cases only 4 mm. in diameter.

In five hearts the process of calcification extended beyond the aortic valve into the ring of the mitral valve. When the mitral ring was involved, the process was either confined to the line of attachment of the aortic leaflet of the mitral valve or the degree of involvement was most pronounced in that part of the ring, fading off in degree in the remainder of the valve ring. In six other hearts the deposition of calcium involved not only portions of the mitral ring, but extended

Fig. 5.—Extension of calcareous process from posterior aortic valve leaflet onto mitral ring and ventricular surface of the anterior aortic leaflet of mitral valve; the calcareous material is seen as two finger-like processes extending from the base of the aortic leaflet.

for a short distance onto the ventricular surface of the aortic leaflet of the mitral valve (Fig. 5). Calcification of the mitral leaflet, however, usually was of slight degree and did not interfere with the function of the valve. Even when areas of calcification did exist in the mitral leaflet, there was no evidence of any other defect in the mitral valve. The auricular surface of the mitral valve was always found to be normal; there was no evidence of preexisting endocarditis.

The coronary arteries in all instances, except one, revealed some degree of sclerosis. In fifteen cases the sclerosis in the coronary vessels was slight; in fifteen cases, moderate; in nine cases, marked, and in two cases, extreme. Occlusion of any of the larger branches of the coronary vessels was not found.

The aorta, too, presented a variable degree of arteriosclerosis. It was slight in thirteen cases, moderate in twelve cases, marked in fif-

teen cases, and extreme in two cases. In general, the sclerosis in the aorta was least pronounced in its proximal portion.

Gross examination of the myocardium revealed scattered areas of grayish streaking due to myocardial fibrosis in fourteen cases. The extent of fibrosis varied considerably and was pronounced in several cases. Evidence of gross myocardial infarction was not encountered. Accumulations of fluid in the pleural sacs were found in ten cases. The fluid was always clear and straw-colored, and varied in amount from 1000 to 3000 c.c. There was marked passive congestion of the liver in three cases, atrophy of the parenchyma in five cases, fatty changes in one case, and varying degrees of fibrosis in two cases. The kidneys presented variable degrees of atrophy in six cases, with well-marked sclerosis of the renal vessels in three cases, and infarcts in only one case. In the spleen, evidence of infarction was noted in one case, and marked congestion was noted in two cases.

Three cases were studied bacteriologically. In one case the culture was sterile. Hemolytic streptococci were recovered at necropsy in a case in which the patient died following amputation of a breast. In another case in which the patient died following exploration of a glioma of the brain, *Streptococcus viridans* was recovered from the blood at necropsy.

*Microscopic Studies.*—Sections were taken in each case from: (1) the interventricular septum, just below the aortic valve; (2) the left auricle, just above the mitral valve; (3) the aortic valve, including the valve ring; and (4) the root of the aorta. The sections were stained with hematoxylin and eosin, and a number of sections of the valves were stained for fat with Scharlach red. Although difficulty was experienced in cutting some of the sections of valves, decalcification was not necessary; an old microtome knife was used, and satisfactory preparations were made.

Sections of the interventricular septum and of the auricular muscle revealed, as the most prominent feature, hypertrophic changes in the muscle fibers. Occasionally increase in the amount of interstitial tissue was found, but this was never marked. Varying degrees of sclerosis of the myocardial vessels were noted in most sections. In one case there was marked sclerosis and calcification of one of the branches of the coronary artery, leading to almost complete occlusion of the lumen. Aschoff bodies were not found. With the exception of one case, cellular infiltration indicative of an inflammatory reaction was not encountered.

Sections of the root of the aorta usually revealed only pathological changes such as are to be found in any group of cases in which the ages correspond to those in our series. Thus, there occurred some

increase in the connective tissue in the media, with hyalinization, and in some instances evidence of arteriosclerosis and deposits of calcareous material.

In eight cases, sections of the proximal portion of the arch of the aorta revealed varying degrees of cellular infiltration. In four of these cases the degree of infiltration was extremely slight, consisting of small, focal collections of lymphocytes, endothelial leucocytes, and an occasional plasma cell. These collections of cells occurred only in the adventitia and usually surrounded small capillaries or were in close proximity to them. The smaller blood vessels in the adventitia of these aortas revealed proliferation of the endothelium, which in some cases resulted in almost complete obliteration of the lumen. The larger arterioles presented thickening of the wall by fibrous tissue. The aorta in another case revealed several small foci of perivascular infiltration, and associated infiltration in the aortic valve was found. This cellular exudate was situated in the fibrous valve ring and was composed of a fairly dense collection of cells, predominantly lymphocytes, an occasional plasma cell, and an occasional endothelial leucocyte. These cells were collected about the capillaries and were also spread diffusely throughout the tissue of the valve ring. Endothelial proliferation in the capillaries, within this valve ring, was a prominent feature. Within the aortic valve, near its base, there was a large, irregular mass of calcareous material which was, however, separated from the exudative cellular infiltration in the valve ring, by a narrow rim of partially hyalinized fibrous tissue which represented the base of the cusp. Old, practically acellular, and somewhat hyalinized fibrous tissue, surrounded the entire mass of calcareous material, so that nowhere did it extend onto the surfaces of the valve. A section of the myocardium, in this case, did not present evidence of an inflammatory reaction. The perivascular distribution of the cellular exudate, and the proliferative endothelial reaction within the capillaries, both in the valve ring and in the adventitia of the aorta in this case, was extremely suggestive of the pathological reaction to syphilitic infection. In a review of the clinical record in this case it was noted that there existed a suspicion of previous syphilitic infection, but this could not be confirmed. The patient also gave a history of recurrent attacks of "rheumatism." From the evidence at hand we look on the histopathological pictures in the aorta and in the aortic valve ring in this case as probably due to syphilis. In the other cases in which small focal collections of cells occurred in the aorta, sections of the valves and of the myocardium did not present evidence of an inflammatory reaction.

In the remaining three of the eight cases in which infiltration was noted in the aorta, the degree of this inflammatory reaction was pronounced. In one of these three cases the cells were closely aggre-

gated in one section of the adventitia. There were, in addition, scattered through the adventitia, a smaller number of small lymphocytes and an occasional endothelial leucocyte. Endothelial proliferation of capillaries was not observed in this section. Sections of the aortic

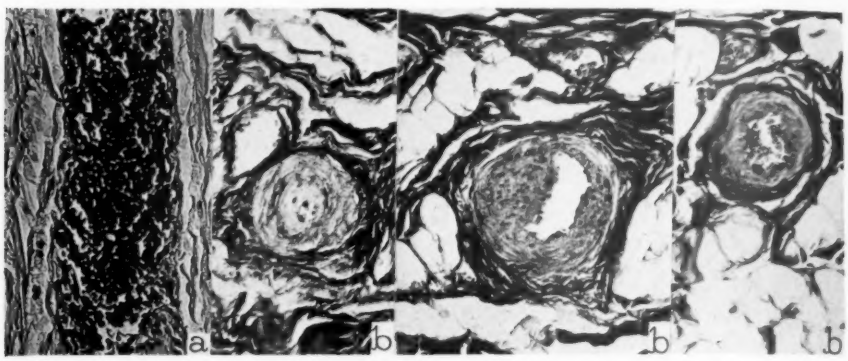


**Fig. 6.—(*a*) Proximal portion of aorta in a case of calcareous aortic valvular disease; perivascular round-cell infiltration in the adventitia (hematoxylin and eosin ×185); (*b*) intimal proliferation in the vasa vasorum within the adventitia (van Gieson's stain ×175).**

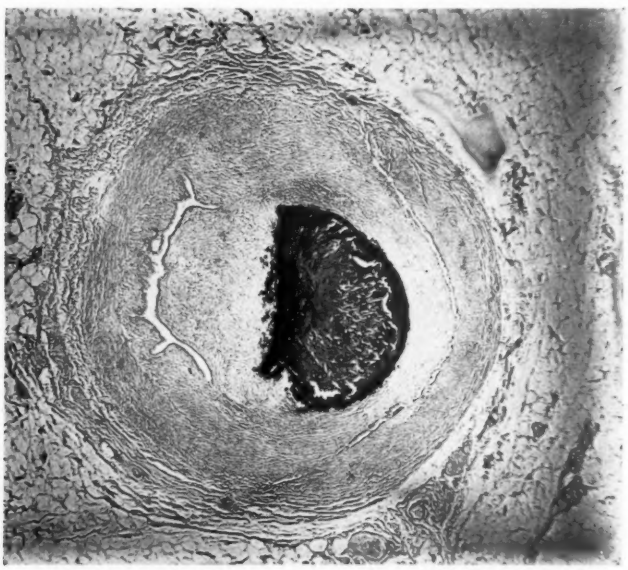

**Fig. 7.—Marked intimal proliferation with thickening of the wall and narrowing of the lumen of one of the arteries within the adventitia of the aorta; also calcareous infiltration within the arterial wall and canalization (hematoxylin and eosin ×30).**

valve and of the myocardium did not reveal evidence of inflammatory reaction; neither was there a clinical history of rheumatic fever or of syphilis. In another case diffuse and perivascular lymphocytic infiltration in the adventitia and endothelial proliferation in the capillaries were associated with perivascular lymphocytes in the

media, which also showed scattered areas of degeneration. The microscopic appearance was extremely suggestive of syphilitic aortitis. This occurred in a case in which a strongly positive Wassermann reaction was found without other clinical evidence of the infection. In this case, too, the syphilitic nature of the aortitis hardly can be doubted. The myocardium revealed no evidence of an inflammatory reaction.

The third case in which pronounced infiltration of the aorta was noted was that of a woman aged twenty-five years, who did not give a history either of syphilis or of rheumatic fever, and who died of a brain tumor. There was marked lymphocytic perivascular infiltration in the adventitia of the aorta, and a pronounced degree of endarteritis

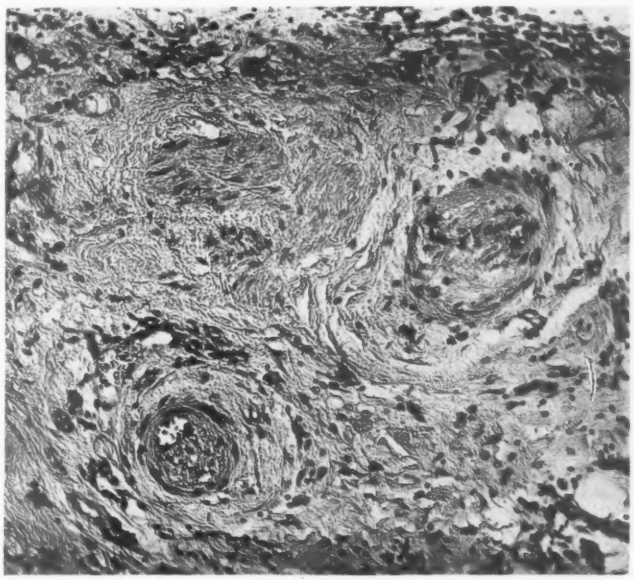

Fig. 8.—Aortic valve ring in a case of calcareous aortic valvular disease; marked endarteritis with tendency to obliteration of the lumina of the capillaries and beginning hyalinization of the surrounding connective tissue (hematoxylin and eosin ×125).

of the smaller vasa vasorum, leading to complete obliteration of the lumina of many of them (Fig. 6). In one of the larger arteries within the adventitia of the aorta, at the level of the insertion of one of the aortic cusps, there was a most marked degree of intimal proliferation, which resulted in marked thickening of the wall of the artery, and encroachment on the lumen of the vessel; the lumen was reduced to a narrow slit only. The tissue of this thickened arterial wall had lost its cellular character and had assumed a hyalinized appearance. Within this thickened wall, on one side, there was a mass of calcareous material, and peripheral to it several narrow channels which appeared to be evidence of canalization within the thickened intima. There was no evidence of inflammatory reaction about this artery (Fig. 7). Sec-

tion of the aortic valve in this case revealed also pronounced inflammatory reaction within the valve ring. Endothelial proliferation of the smaller vessels in the valve ring was extremely pronounced; the lumina of many of the capillaries were almost completely obliterated by endothelium (Fig. 8). In the surrounding fibrous tissue there were advanced degeneration of the fixed cells; diffuse, but scanty, infiltration of lymphocytes, plasma cells, and endothelial leucocytes, and, in foci, proliferation of the fixed connective tissue cells. Irregularly distributed within the valve cusp, near its base only, were many irregular masses of calcareous material which lay embedded in almost acellular, homogeneously hyalinized connective tissue. It was rather striking to observe a zone of hyalinized connective tissue constituting the base

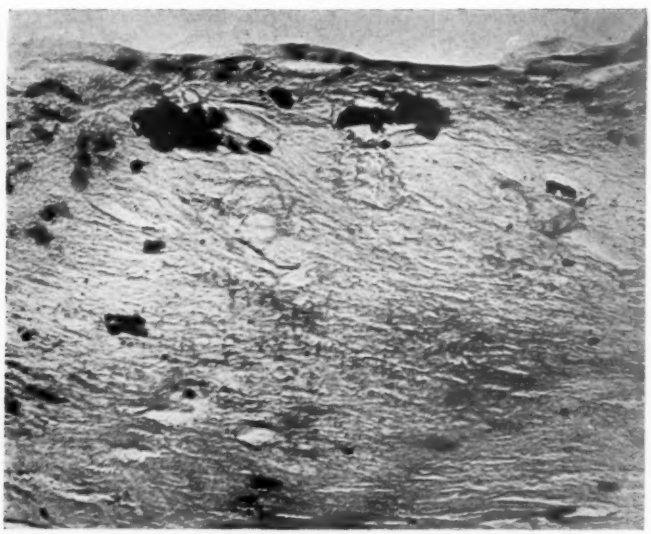

Fig. 9.—Cross-section of aortic valve leaflet; calcareous material deposited within the subendothelial and hyalinized connective tissue near the aortic surface of the cusp; cellular infiltration is absent (hematoxylin and eosin ×225).

of the valve, separating the seat of the inflammatory reaction in the valve ring from the masses of calcareous infiltration in the valve cusp. We were impressed also by the relatively acellular appearance of the entire valve cusp, of which the thickened fibrous tissue throughout was the site of advanced hyaline degeneration.

Sections of the aortic valves revealed deposition of calcareous material, varying in degree from only small, dust-like, calcareous particles, to massive, nodular infiltration with calcium salts. Where only small amounts of calcareous infiltration were found, they were characteristically in the subendothelial connective tissue, near the aortic surface of the valve leaflet (Fig. 9). The endothelium appeared to be intact, and maintained its regular outline. With more marked degrees of infiltration, there was invasion of the middle layer of fibrous tissue in

the valve leaflet and subsequently extension of the process very near the aortic surface of the cusp. This produced bulging on the aortic surface, distorting the regular outline of the surface endothelium, but often leaving it intact (Figs. 10 and 11). Only in those cases in which extremely massive calcareous infiltration occurred was destruction of the surface endothelium found; the calcareous nodules were covered

Fig. 10.—Cross-section of aortic valve leaflet, with valve ring and aorta; the calcareous masses are seen in the middle of the leaflet, extending to the aortic surface; bulging on the aortic surface of the cusp and beginning retraction of the leaflet (hematoxylin and eosin ×6.5).

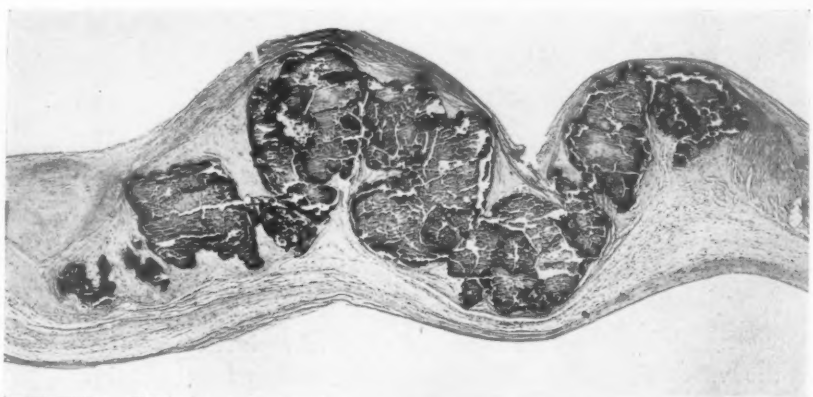

Fig. 11.—Section through an area of calcareous infiltration within a leaflet of an aortic valve; calcareous deposition within the upper portion of the middle zone of old hyalinized connective tissue and beginning destruction of endothelial covering; cellular infiltration is absent (hematoxylin and eosin ×23).

by thin layers of fibrin. Surrounding the masses of calcareous material, was the thickened fibrous tissue of the valve, which was practically acellular and in many cases hyalinized. Scattered within the fibrous tissue, and particularly in the periphery of calcareous nodules, there were variable amounts of lipoid material which in foci formed rather large globules. Usually there was complete absence of cellular

infiltration in the affected valves; evidence of inflammation was entirely absent. However, in five of the forty-two cases, sections of the aortic valve revealed small collections of lymphocytes and endothelial leucocytes in the valve cusps, usually in the base of the valve, in the proximity of regions of calcareous infiltration. In one of these sections there was in the midst of the lymphocytes one giant cell. A section of the aortic valve in one case revealed ulceration of the endothelium near one of the calcareous nodules, and the presence of a small, partially organized vegetation in which there were still numerous lymphocytes and occasional polymorphonuclear leucocytes.

In view of the observation of striking obliterative vascular changes in the aortic valve rings in two of our cases, we directed further attention to the study of these rings in a number of cases with the view

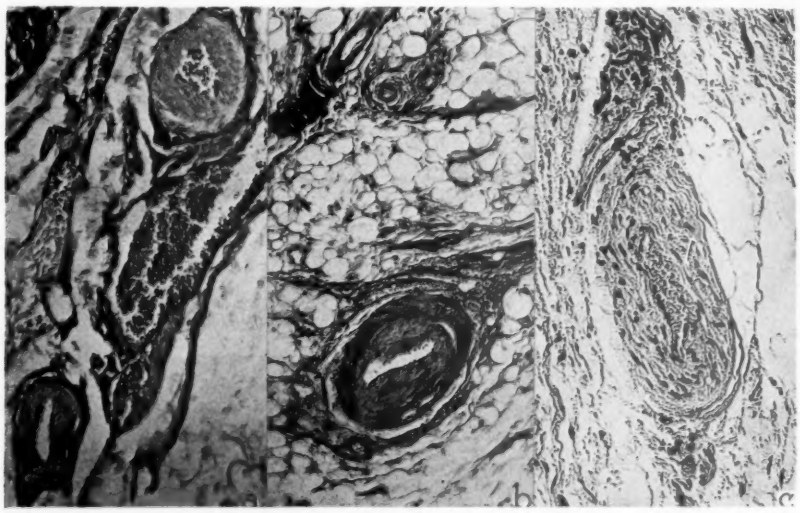

Fig. 12.—(*a*) Section of aortic valve ring in a case of calcareous aortic va'vu'ar disease; thickening of the walls of arterioles and narrowing of their lumina (van Gieson's stain ×150); (*b*) and (*c*), thickening of the walls of arterioles within the aortic valve rings in two other cases of calcareous aortic valvular disease (van Gieson's stain ×100 and hematoxylin and eosin ×215, respectively).

of determining the possible relationship of endarteritis in the vessels of the valve ring to the pathological changes in the valve. These sections of the valve rings were stained by hematoxylin and eosin, by the van Gieson method and by the Weigert elastic tissue stain. Of the sixteen cases studied from this standpoint, only a small number showed any striking vascular changes. Not in any case could we observe vascular changes as pronounced as those noted in the case which attracted our attention to this phenomenon, the case we have already described in detail. However, in four cases there was pronounced thickening of the walls of the smaller arterioles and proportionate narrowing of their lumina (Fig. 12). Changes in the intima were usually not marked, the thickening apparently resulting mainly from pro-

liferation in the media. Occasionally we observed endarteritis of the capillaries associated with arteriosclerotic changes in the arterioles. In one case, the fibrous tissue of the valve ring was hyalinized and almost avascular, but there were present whorl-like masses of poorly staining, flattened cells, which did not present lumina, but nevertheless suggested the appearance of completely obliterated capillaries, although their identification as such, with certainty, was impossible. In other sections the valve ring contained fairly numerous, normal-appearing vascular channels, contrasting markedly with sections of the valve rings from other hearts in which the connective tissue was practically avascular. Although equivocal, these observations of the vascular changes in the valve rings merit consideration in a study of the pathogenesis of this form of valvular disease.

It is interesting to consider why this lesion is so infrequently associated with signs of cardiac failure, even when it appears to have existed for a long time. First of all, the degree of stenosis and insufficiency of the aortic valve is probably relatively small except in the more advanced cases. The best evidence of that fact is the comparison of the relatively low cardiac weights encountered here with those found in cases of aortic stenosis and insufficiency due to other causes.

The left ventricle seems to have a large inherent capacity to compensate for the effects of aortic stenosis when compared with the reaction of the right ventricle to mitral stenosis. Willius found that patients with aortic stenosis survived, on the average, thirteen years longer than patients with mitral stenosis. It must be admitted, however, that mitral stenosis produces more widespread effect on the heart as a whole than does aortic stenosis.

When this group of patients is considered as a whole, there is little evidence that other factors coexist, leading to injury of the left ventricle. There is practically no evidence of myocarditis in the ventricles of these patients. The degree of coronary disease appears to be no greater than one would expect to encounter in a group of normal patients of the same sex and age. The number of patients in this group who had abnormally high blood pressures is small. In most cases the increase is chiefly in the systolic pressure, with relatively low diastolic readings, such as commonly are found in cases of hypertension associated with sclerosis and inelasticity of the aorta.

Finally, there are few disturbances of rhythm complicating these aortic lesions to interfere further with cardiac efficiency. Auricular fibrillation occurred in only seven cases, and in three of these hyperthyroidism was the probable cause.

The infrequency with which this condition of calcareous disease of the aortic valves was recognized clinically must depend in part on the fact that there are often few, and in some cases, no symptoms of cardiac disease associated with it. Obviously the first step in making

the diagnosis is the knowledge that such a lesion can exist and that it may be suspected especially in a patient who is more than fifty years old, and particularly if the patient is a man. This study indicates that the observations on physical examination will be those encountered in aortic stenosis or regurgitation from other causes. The murmurs heard in these cases usually are systolic in time, rough or musical in quality, maximal over the aortic region but having wide transmission over the precordium and to the vessels of the neck. If a painstaking attempt is made, it is believed that a thrill at the base of the heart can be demonstrated in a large proportion of these cases, and its demonstration fortifies the diagnosis greatly. In those cases in which regurgitation occurs, the usual diastolic murmur along the left side of the sternum will be heard.

From the standpoint of prognosis, these cases have both a favorable and an unfavorable aspect. On the favorable side is the fairly conclusive evidence that the lesion can exist over a long period without producing significant cardiac symptoms. On the unfavorable side is the fact that a certain proportion of the patients die suddenly; although until the time of death they appear to be in normal health. Certainly, in general, the prognosis in aortic stenosis of this type appears to be much more favorable than that of mitral stenosis.

## COMMENT

On the basis of the pathological processes observed in the aortic valves involved by these peculiar calcareous deposits, one would be led to conclude that degenerative processes, probably on an arteriosclerotic basis, played an important and possibly a predominant part in the pathogenesis of this lesion. In support of this viewpoint must be mentioned the common occurrence of calcareous and hyaline degeneration of the valves and in some cases, the presence of obliterative vascular changes in the valve ring, in the absence usually of an inflammatory reaction. When the lesion is encountered at necropsy, the subject is usually a male more than fifty years old.

However, in a consideration of the etiology and pathogenesis of calcareous disease of the aortic valves, it is important to bear in mind that the lesions described here, in many cases, had begun many years before. It is obviously difficult to visualize, from pathological changes observed at the end of a disease process, the pathological process which occurred at its inception.

The possibility that this lesion may have an inflammatory basis receives some support from the observation of inflammatory processes in the aorta, in the aortic valve, or in both in eleven of our cases. This is particularly exemplified by one case which we described in detail, that of a woman twenty-five years old, who presented suggestive evidence of an inflammatory basis for typical calcareous aortic

valvulitis. In such a case, a rheumatic or other infectious etiologic basis for the affection must be strongly suspected, although the clinical history did not record episodes of infection. The death of this patient at an early age, and from a cause entirely independent of the cardiovascular lesion, may explain why an inflammatory process was still apparent in the affected valve and aorta at necropsy.

If it is assumed that this lesion has an infectious basis, then two possible mechanisms in its production are suggested by the observations made in this study.

1. It is possible that rheumatic fever may be the basis of many of the cases. According to this view, one assumes that this lesion begins as ordinary rheumatic aortic valvulitis and that the calcareous noninflammatory lesion which is usually observed at necropsy represents a more or less completely healed lesion. This conception receives some support from a case of typical calcareous aortic valvular disease which came to necropsy since this study was completed. The patient, a man forty-five years old, gave a history of having had rheumatic fever and chorea at the age of twelve years, and he had had rather definite evidence of a valvular heart lesion at the age of twenty-five years, because of which he was refused life insurance. On clinical examination, the arterioles of the fundus oculi were normal. Only a negligible amount of sclerosis was observed in the coronary arteries and aorta at necropsy. It is difficult to evade the impression that there existed, in this case, an etiologic relationship between the rheumatic fever and the calcareous aortic valvular disease. If this process is accepted as being of rheumatic origin, then one must recognize that the distribution of the lesion in the valve is certainly unlike that usually observed in rheumatic valvulitis, particularly in respect to the freedom of involvement of the free margin of the cusps.

2. It is possible that this lesion results from an inflammatory process involving the arterioles of the aortic valve ring, leading to endarteritis in the nutrient arteries of the aortic valves, resulting in ischemia. This process is particularly suggested by the observations in the case of the woman twenty-five years old, which has been described.

Finally, it is possible that marked narrowing and possibly obliteration of the arterioles of the aortic valve ring, occurring as a part of ordinary generalized arteriosclerosis or as a selective, localized arteriosclerotic process might likewise produce ischemia of the aortic valves leading subsequently to degeneration of and calcareous deposits in the valves. According to this assumption the primary pathological changes in the valves would be due essentially to ischemia, possibly of insidious onset and of a slowly progressive character. This conception, too, might explain certain anatomical peculiarities of the pathological process such as the usual beginning of the process near the commissures of the valves, the more frequent fusion of certain valve

leaflets than of others, and the peculiar selective extension of the process in certain cases to the anterior (aortic) leaflet of the mitral valve, if there should exist certain peculiarities in the distribution of the vascular radicles of the blood supply to the aortic valve. Involvement of the arteria anastomotica auricularis magna, as described by Kugel, supplying branches to the aortic cusp of the mitral valve, occasionally to the aortic valve, to the commissures, and to the base of the aorta, might account for the pattern-like confinement of the pathological process to certain preferential regions; namely, the commissures, valve rings, and, in certain instances, the aortic cusp of the mitral valve. However, more detailed knowledge regarding the blood supply of the aortic valves is needed before one can determine their relation to the pathological process in the aortic valve described here.

In the development of the lesion any of these mechanisms, if they should prove to be correct, appear to satisfy certain conditions believed to permit the deposition of calcium, in that they are capable of initiating degenerative changes in the affected valve. We cannot enter here into a detailed consideration of the process of calcification, except to remark that aside from the pathological changes in tissues which make them suitable soil for the deposition of calcium, there probably exist certain chemical or physicochemical factors which either favor or impede the process. It is, however, well established that under certain pathological conditions calcification is likely to occur. Wells wrote: "It may be said that any area of dead tissue that is not infected, and that is so large or so situated that it cannot be absorbed, will probably become infiltrated with lime salts. Most frequently calcified, next to totally necrotic tissues, are masses of scar tissue that have become hyaline subsequent to the shutting off of circulation in the scar by contraction of the tissue about the vessels." With respect to the calcification which supervenes in the process of atherosclerosis of the aorta and other large vessels, the views expressed by Aschoff are probably most widely accepted. It must be recalled that as the fundamental pathological changes in that process Aschoff assumed the presence of a degenerative process of the supporting substance of the vessel wall, with subsequent processes of precipitation, especially of lipoid substances, and the subsequent transformation to calcium compounds. Although grossly, and in sections stained by hematoxylin and eosin, atheromatous changes in the valves are not recognizable, accumulation of lipoid material in association with hyalinization and calcification is nearly always evident when sections of the valves are appropriately stained for fat. Thus the appearance of the degenerative process in these valves and in atherosclerosis bear a close resemblance.

We can find no evidence to suggest that this process is the end-result of healed bacterial endocarditis, although we realize that healing in

bacterial endocarditis may result in varying degrees of calcification. In this connection, it is significant to observe the infrequency of a history suggestive of previous endocarditis, the absence usually of vegetative endocarditis, either active or healed, and the rare occurrence of infarction in the kidneys and spleen in these cases. Moreover, such a series of presumably completely healed lesions of bacterial endocarditis is not compatible with our present conception of this disease.

Despite the occurrence of histopathological data suggestive of syphilis in several of our cases, it is obviously impossible to suggest that syphilis frequently plays a part in the etiology of this form of valvular disease. Indeed, it is recognized that in the most commonly observed valvular lesions caused by syphilis, calcification is usually not a prominent feature.

The possibility that the valvular lesion is the result of thrombosis on the surface of the valve, with subsequent organization and calcification of the thrombus, suggests itself. However, in the earliest stages of the process, hyalinization of connective tissue, and calcification, occur characteristically within the substance of the aortic valve ring and in the connective tissue of the cusp beneath the endothelium which remains intact. It is only in the far advanced stages of the process, when the calcareous deposits become large, that they cause secondary changes in the endothelium, finally breaking it, the calcareous material then projecting on the surface of the valve.

More conclusive evidence bearing on the various mechanisms of pathogenesis considered here will probably come through studies of early cases, cases in which histories are complete and clinical observations have been made over long periods of time, and through a study of the degree and distribution of calcareous deposits in aortic valves associated with undoubted cases of rheumatic mitral endocarditis.

## SUMMARY AND CONCLUSIONS

Although calcareous aortic valvular disease is relatively uncommon, it should be suspected more often when patients, particularly elderly men, present certain clinical phenomena which have been considered here. Heretofore, a clinical diagnosis of this condition rarely has been made. This is due to the tendency of the condition to cause few subjective symptoms, apparently the result of the remarkable capacity of the heart to compensate for the mechanical circulatory disturbance which this lesion produces. Lack of clinical awareness of this condition undoubtedly is a great factor tending to errors in diagnosis in this form of valvular disease.

Pathologically, the lesion is characterized by a tendency to hyalinization of the connective tissue, deposition of lipoid material in the aortic valve ring and in the aortic valve, and subsequent calcification of the affected tissues.

The etiology and pathogenesis of this form of valvular disease could not be determined with certainty. Clinical and pathological data indicate that the lesion in some cases may have an inflammatory basis, whereas in others it may represent the result of a noninflammatory degenerative process.

Certain features suggest that ischemia due to diminution of the vascular supply of the affected tissues may be the basic pathogenic factor productive of hyalinization and of other degenerative changes which subsequently proceed to calcification.

Further study of the blood supply of normal valves, and of the relationship of vascular lesions to this and to other forms of endocarditis, seems indicated.

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# PARTIAL BUNDLE-BRANCH BLOCK: A THEORETICAL CONSIDERATION OF TRANSIENT NORMAL INTRAVENTRICULAR CONDUCTION IN THE PRESENCE OF APPARENTLY COMPLETE BUNDLE-BRANCH BLOCK*

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BUNDLE-BRANCH block, complete or incomplete or defective intraventricular conduction, has long been considered an inalterable disturbance, the result of anatomical changes and therefore a reliable sign of very serious myocardial damage. Cases with from slight to complete conduction defects are of fairly frequent occurrence, while examples of partial or functional bundle-branch block are rare but nevertheless do occur in any medical clinic where a large number of patients with heart diseases are examined electrocardiographically.

In the majority of cases, the altered mechanism is considered to be permanent and complete. Partial or transient intraventricular conduction disturbances with which this paper deals, are relatively uncommon apparently because of the fact that in contrast to the situations in partial auriculoventricular block the intraventricularly blocked ventricle will promptly receive an impulse from the other ventricle under all but extraordinary circumstances.

Prognostically electrocardiographic findings indicating defective intraventricular conduction, especially if persistent, are significant of a grave myocardial damage. If the abnormalities are transitory, the prognosis is much better. This is to be especially emphasized when there is any consideration whatsoever of the subjection of a patient with such a disorder to any unusual diagnostic or therapeutic procedure such as intravenous injection or surgical operation. The latter procedure is likely, in itself or as a result of the anesthetic, to produce blood pressure changes or shock, or further adversely to affect the myocardium by depression.

In the presence of bundle-branch block the heart is laboring under the burden of an asynchronous action of the two ventricles in addition to the effects of the widespread myocardial damage which locally has produced the defective intraventricular conduction. Apparently in such a heart in the presence of concomitant depression ahead and recovery behind, as the impulse spreads from the one ventricle to which it is conducted through the septum to the blocked-off ventricle, there

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is likely to be established on relatively slight provocation with any even slight additional depression a circus rhythm which may result in fatal ventricular fibrillation.

The possible transient nature of these defects which have such a grave significance warrants emphasis. The consideration and the recognition of the fact that the block may be partial, though usually permanent, but that it is by no means always so, is important. The temporary or functional block is the result in a large measure of circulatory, nutritional or oxemic disturbances in the conduction system rather than of inalterable organic changes.

## PREVIOUSLY REPORTED CASES

There have been reported about ten instances in which electrocardiographic evidences of changes in intraventricular conduction time have been recorded at different times of observation. After reviewing these cases we wish to record five more of this same type. Besides this we have had three most unusual cases in which we have been able to record sudden transitions from complete bundle-branch block to normal intraventricular conduction time for transient periods as the result of indirect vagus effects.

Lewis[1] as early as 1913, found a case in which transient block occurred in the right branch of the His bundle during a febrile attack. It was noted on the third day of the patient's illness when the fever ranged between 99° and 100.5°. It was absent on the fourth day and thereafter. Lewis' patient, a bookbinder, aged thirty-two years, had had dyspnea on walking for six years, an aching precordial pain for months, and a general "seedy" feeling which suggests the possibility of his having had a complicating acute endocarditis. The patient had an enlarged heart with free rheumatic aortic regurgitation. The electrocardiographic curves published with this case showed a shift in the origin of the T-waves which we might now consider very suggestive of coronary disease. Another subsequent curve interpreted as physiological is suggestive in the light of recent investigation of an incomplete bundle-branch block, which means some persistence of the defective intraventricular conduction. The QRS interval changed from 0.13 second to 0.10 second.

The same patient is commented upon by Carter[2] as Case 12 in his series. Carter's Case 20 was the first in which the electrocardiogram of the individual was obtained before as well as after the development of defective intraventricular conduction.

Cohn and Lewis,[32] in a detailed microscopical study, found no recognizable pathological lesions in the complete serial sections of the conduction system of each of four cases. The discrepancy in these four instances between electrocardiographic and pathological findings

seems evidence sufficient, as the authors point out, that definite functional changes are not dependent absolutely upon recognizable anatomical changes. In one instance large blood spaces in and about the conduction system and pressure from these was considered to be a probable contributing factor in the precipitation of the bundle-branch block that had been recorded during the life of the patient.

Robinson,[4] in further support of the functional nature of such changes in intraventricular conduction, reported another case in which the defective intraventricular conduction was clearly not based entirely on pathological lesions. He suggested that the disturbance was the result of "functional fatigue" and advanced the hypothesis that the interference was due to the accumulation of acid metabolites in the intraventricular conduction system. These chemical changes he felt, were the result of nutritional disturbances due to sclerosed coronary arteries and perhaps to other lesions of the myocardium.

Krumbhaar[5] commented upon Lewis' unique case and presented one of his own, which was of further interest in that defective intraventricular conduction was observed in the process of development. His observations were of a man, seventy-six years old, with arteriosclerotic heart disease and mild anginoid attacks. His first examination showed marked left ventricular predominance with a QRS interval of about 0.10 second and an upright T-3, which signs we would today consider as evidence of incomplete bundle-branch block. One month later the electrocardiographic study showed complete bundle-branch block which persisted and was apparently permanently established.

Willius and Keith[6] were fortunate enough to observe three cases in which there were conspicuous changes in the degree of the intraventricular conduction defects. All three of the cases were considered to be incomplete bundle-branch block. On the first observation in the first two, the QRS intervals and the characteristic T-wave changes strongly suggest that the bundle-branch block was practically complete. These authors emphasize the importance of recording these transient changes and explain them on the basis of myocardial fatigue, exaggerated by acute cardiac failure. The first case showed very little evidence of congestive failure. These cases again illustrate the fact that apparently profound disturbances in intraventricular conduction may be evanescent and the prognosis therefore would be more hopeful.

Von Kapff[7] considered intracardiac hemorrhage as the most likely cause of the temporary intraventricular block in his case. Slight T-wave changes following the ectopic beats were considered evidence of a persistent slight conduction defect. Myocardial infarction must be considered a possible precipitating factor in this case as well as in some of the other cases.

Baker[8] observed a case of transient bundle-branch block which disappeared with a slowing of the heart rate and failed to reappear with a rise in rate during exercise in which the administration of oxygen was carried out.

Leinbach and White[9] reported a rare instance of transient two-to-one bundle-branch block, a phenomenon previously observed by Stenström, whose records, however, are published by these authors. The authors do not discuss the two instances of the unusual mechanism other than to comment upon the rarity of the condition.

Slater[10] recently published a case of three-to-one and four-to-one partial bundle-branch block and discussed the theory of the subject at some length.*

## COMMENTS

This review comprises the cases of transient bundle-branch block that appear in the literature up to the present time and to this series we will add our eight cases. It is to be noted that most of the previously reported cases usually presented defective conduction at one examination with later improvement, or less commonly, the reverse. The transitions were gradual, a result either of prolonged rest or of therapeutic measures or indiscretions. In a few instances the changes were abrupt from normal to abnormal intraventricular conduction, a result of progressive degenerative changes that suddenly became rapid as a result of infection or intracardiac circulatory disturbances, so that the defective intraventricular conduction or bundle-branch block was observed in the process of rapid development. In the one case reported, infection with fever may well have produced those essential temporary changes in the conduction tissues of the primary branches of the His bundle, which contributed to the transient block. In other cases changes in the vagus tone played a part. In some cases cardiac infarction as a result of coronary thrombosis has probably been the exciting cause. In most of the cases progressive myocardial exhaustion, anoxemia, functional fatigue, the accumulation of products of cell metabolism and congestive failure, were apparently precipitating factors.

This all supports the contention of Cohn and Lewis,[32] proved by their careful anatomical studies, that the electrocardiographic findings are not necessarily dependent upon visible histological alterations. The branches of the His bundle, just as the main bundle itself, may be the seat of functional conduction disturbances even in the absence of microscopically recognizable pathological changes.

*After this was written an interesting paper by Wolff, Parkinson and White (AM. HEART J. 5: 685, 1930) has appeared in which they report eleven cases of bundle-branch block, mostly in otherwise healthy young people with paroxysms of tachycardia or auricular fibrillation. Abrupt transitions occurred spontaneously or as a result of exercise or atropinization from bundle-branch block with unusually short P-R intervals (0.1 sec.) to the normal physiological electrocardiogram with P-R intervals of normal duration. Such short P-R intervals during the periods of bundle-branch block are not characteristic of our own cases which probably depend upon a different mechanism.

## THE PRESENT STUDY

The first three cases, those which we particularly wish to emphasize in this paper, are unusual in that seemingly profound intraventricular conduction disturbances with apparently complete bundle-branch block, were observed to change within one beat to complexes of an entirely different and absolutely normal contour, with normal short QRS intervals and vice versa. The importance of the observations lies in the fact that these records are strong evidence that the complete intraventricular conduction disturbances may be precipitated by changes in vagus tone and are thus in a large part functional in character. It seems highly improbable that anything but a nervous, chemical or acute mechanical pressure change could take place and give such results within the period of one heart cycle. Slight stretching or dilatation of the heart from increased intraventricular pressure shifts in an already disturbed intracardiac circulation, with perhaps the engorgement of the venous channels in and about the specialized conduction tissue, could all be theoretically held accountable for such sudden transitions in form of the ventricular complex. A narrow lesion which in itself does not obstruct the passage of impulses might conceivably be present in the conducting pathway and yet cause no delay of the impulse until one of the factors suggested precipitates block.

## THREE INSTANCES OF SUDDEN INTRAVENTRICULAR CONDUCTION TRANSITIONS CAUSED BY INDIRECT VAGUS EFFECTS IN PART AND BY ANOXEMIA AND FATIGUE FOLLOWING EXERTION

The first three cases are all of sudden transition from complete bundle-branch block to normal intraventricular conduction which we observed in patients following the taking of a deep breath and the holding of it for from a few seconds to a minute with resulting indirect vagus effects. In one instance a slight amount of exertion was necessary before the intrathoracic and intracardiac pressure shifts were sufficient to produce the significant changes.

CASE 1.—A mother superior, aged fifty-five years, was referred to one of us for electrocardiographic and cardiac study by Dr. Joseph Larimore. This case has been briefly described in a series of unusual disturbances of the mechanism of the heart beat, reported by Dr. F. N. Wilson and one of us.[11] She had had a most unusual symptom complex. In January, 1920, she began to have weakness and indefinite abdominal distress. The spleen and the liver were found enlarged, as they had been six months previously. The white blood count revealed 27,000 leucocytes per cubic millimeter, 85 per cent of which were polymorphonuclear neutrophils. Very little history was elicited that was diagnostic of any of the usual syndromes, and no other abnormal findings were noted at that time.

The patient had had a "bilious attack" with slight icterus about fifteen years previously. She suffered no further illness until three years before admission when she had an attack of acute arthritis in the right knee. In the next year she began

to have attacks of severe pain in the chest, which seemed to have been of cardiac origin. The attacks recurred frequently during a period of three months and then spontaneously subsided.

In August, 1919, she suffered a heat stroke and had a recurrence of the acute attack of severe pain in the chest. Within a month an ulcer appeared on the right great toe and persisted for a month. Masses were found in the abdomen for the first time, and because of the presence of leucocytosis and a fever, along with the mass in the left flank, the patient was thought to have a perinephric abscess. An exploratory operation through the posterior route, however, revealed a normal kidney. Further exploration was then done through the abdominal wall anteriorly, and the spleen was found to be very large and completely infarcted. There was practically no normal splenic tissue left, and the organ was therefore removed. A left-sided pneumothorax developed after the operation, but otherwise postoperative convalescence was uneventful.

Gradual general clinical improvement continued until March, 1920, when there appeared an enlargement of the abdomen due to the accumulation of ascitic fluid. The intraabdominal tension became so great that the abdomen had to be tapped at intervals of two weeks. At each tapping two and one-half liters of straw colored fluid of low specific gravity were removed. The pleural cavities were found to contain similar fluid. After a third tapping, a diarrhea intervened, and this was apparently sufficient so to upset the water balance that the fluid temporarily stopped accumulating in the serous cavities.

In May, 1920, there was an acute left axillary adenitis associated with edema of the left arm. This cleared up spontaneously within a week. The patient had several attacks of acute gastro-enteritis at varying intervals. The leucocytosis persisted. The Wassermann reaction was negative, as was also the complement-fixation test for tuberculosis. Gradual improvement followed so that within a year the patient was able to reassume her heavy administrative duties and suffered only from constipation.

An intense pruritis over the entire body with slight edema of the ankles in the evening was occasionally troublesome. The liver edge remained about 6 or 8 centimeters below the costal margin. Urine contained a trace of albumin, and a few granular casts. The hyperleucocytosis of the blood persisted. A soft systolic murmur was heard in the mitral area; the lungs and pleura, however, were clear. The evidences of renal irritation entirely disappeared. The ascites recurred in disturbing amounts a year after she resumed her work. She was reported to Dr. Joseph Larimore to have died suddenly August 21, 1922, two and a half years after the first electrocardiographic examination.

## COMMENTS ON ELECTROCARDIOGRAMS

During the taking of the electrocardiograms we noticed the long QRS interval and the diphasic T-waves, the evidences of complete bundle-branch block. The downwardly directed complexes of Lead III, although here definitely a part of the bundle-branch block caused us to try the effect of a respiratory test. This is routinely done by us in the presence of left ventricular predominance to determine the part played by the transverse position of the heart. The examination was made by asking the patient to take a deep breath and to hold it. While this was being done and the effects were on, the electrocardiograms were taken. During this maneuver we noticed that a sudden change in the form of the ventricular complex occurred. The slow,

broad QRS of the bundle-branch block was replaced by a sharp, quick deflection of normal contour and normal intraventricular conduction time. The maneuver was repeated several times, and the effects were photographed (Fig. 1). We noted that after a period of from a few seconds to a few minutes the bundle-branch block complexes invariably returned. A study of the curves showed that all the transitions took place suddenly as the rate, decreased by indirect vagus action,

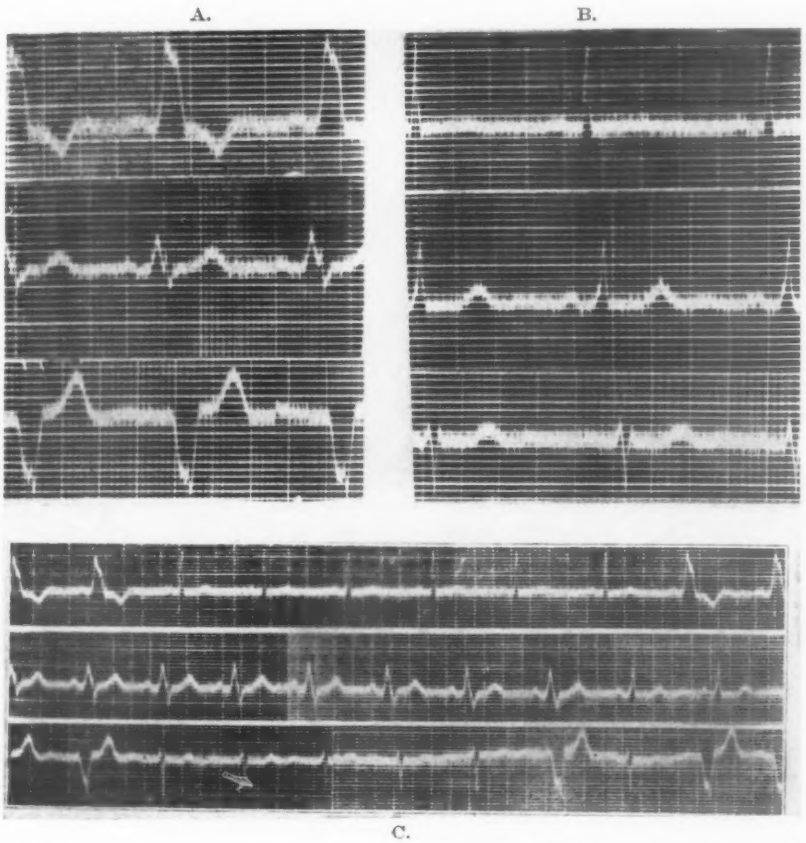


Fig. 1.—Case 1. *A*, Leads from above downward I, II, and III during complete bundle-branch block of the usual type (as all of our cases were). *B*, Leads I, II, and III during normal intraventricular conduction in the same patient after rest. *C*, Leads I, II, and III showing the abrupt transitions from complete bundle-branch block to absolutely normal conduction. See text.

dropped from about 75 to 65 per minute. Occasionally there was an alteration between the block and normal conduction suggesting a two-to-one partial block in the branch of the His bundle. This is shown in the last four complexes of Lead III (lower Fig. 1), although it might be argued that the first broad complex to appear after the normal intraventricular conduction period is a free wall ventricular escape. This, however, is quite unlikely.

The patient was then allowed to return home and to rest for a short period of time. When she was to be returned to the electrocardiographic laboratory, the attendants were instructed to bring her in a wheel chair to avoid the possible fatigue that the walking to the Heart Station may have incurred at the first examination. The curves taken after the rest without exertion showed normal intraventricular conduction. After mild exercise, consisting in lifting a five pound dumbbell in each hand six or eight times with forward and sideward movements of the arms, the bundle-branch block complexes returned, and the respiratory test caused them to disappear temporarily again. Electrocardiograms recorded these facts, and examination of the curves corroborated the suspicion that there had been an extraordinary change from normal intraventricular conduction to a complete bundle-branch block (Fig. 1). There had been a change of the reverse character with exertion probably due to anoxemia of the conduction tissue and a release from the same again on resting.

Case 2.—M. J., a negro woman, cook, aged 47 years, was admitted to Charity Hospital January 22, 1928, complaining of pain through the left chest and in to the back. She had had some dull pain in the abdomen and in the back for two years. During September, 1926, she began to notice some distress in the precordium, palpitation and shortness of breath on slight exertion. The distress became more and more marked and was brought about by less and less exertion. For some months there had been a distinct precordial distress with radiation to the back with the least effort. She had had some morning nausea but no vomiting. Swelling of the ankles and feet had been present for the past few months. Occasionally she suffered from a fainting spell. She became so incapacitated by September, 1928, that it was impossible for her to go up a flight of stairs.

Her father had died at the age of 57 years, her mother at 46 years of unknown causes. She had been married for 28 years but had had no children and no miscarriages. She had had no serious diseases in the past but was not sure whether or not she had had venereal diseases of any type. She chewed tobacco and snuff, used very little coffee and no alcoholic drinks.

*Physical examination* showed a huge, obese negro woman, 69 inches tall, weighing 190 pounds. She was uncomfortable even in the reclining position. The pupils reacted to light and in accomodation. The thyroid and the cervical lymph glands were very slightly enlarged. The neck veins, carotid and subclavian pulsations were slightly increased. The aorta was palpable in the suprasternal notch, and there was a distinct increase in the retromanubrial dullness. The cardiac outline extended 3 centimeters to the right and 14 centimeters to the left of the midsternal line. The apex impulse was just palpable in the fifth interspace in the midclavicular line, 13 centimeters to the left of the midsternal line. The aortic second sound was loudly accentuated and reverberating; the pulmonary second sound seemed to be reduplicated. A soft, systolic murmur was heard at the apex. The blood pressure was 212 mm. systolic and the diastolic sustained 140 mm. of mercury. The arteries were not distinctly abnormal. The lungs were clear and resonant throughout. There was a scar in the midline apparently from a previous gall bladder operation and drainage of the abdomen. Some tenderness was present over the liver. The hepatic border could not definitely be made out. The feet were slightly edematous.

The *laboratory examination* showed urine with 1.010 specific gravity, containing a trace of albumin, a few casts and epithelial cells. The blood chemistry studies revealed a nonprotein nitrogen level of 33 mg. per 100 c.c., a urea nitrogen of

16 mg., a creatinine of 1.2 mg., a uric acid of 3 mg. and a blood sugar of 100 mg. per 100 c.c. The Wassermann reaction was negative. The diagnoses were hypertensive heart disease; arteriosclerotic aortitis, possibly of luetic origin; coronary disease; anginal as well as congestive heart failure.

The *electrocardiograms* (Fig. 2) showed a complete bundle-branch block of the ordinary or common type. The QRS interval measured 0.18 second and the P-R interval 0.20 second. The complexes were broad, slurred, notched, and the T-waves were diphasic, thus completely fulfilling the bundle-branch block criteria. After three days' rest in bed, the electrocardiograms were found to be totally different from the preceding ones. The QRS complexes with an intraventricular conduction time of 0.08 second were recorded. Although normal in respect to the length of the QRS interval, the T-1 and T-2 waves were sharply negative, and there was some slurring in the R upstroke of Leads I and II, and the main deflection was deeply downward in Lead III.

The respiratory test at this time had little if any effect. Exercise, which consisted of a few squats, caused an immediate return of the bundle-branch block com-

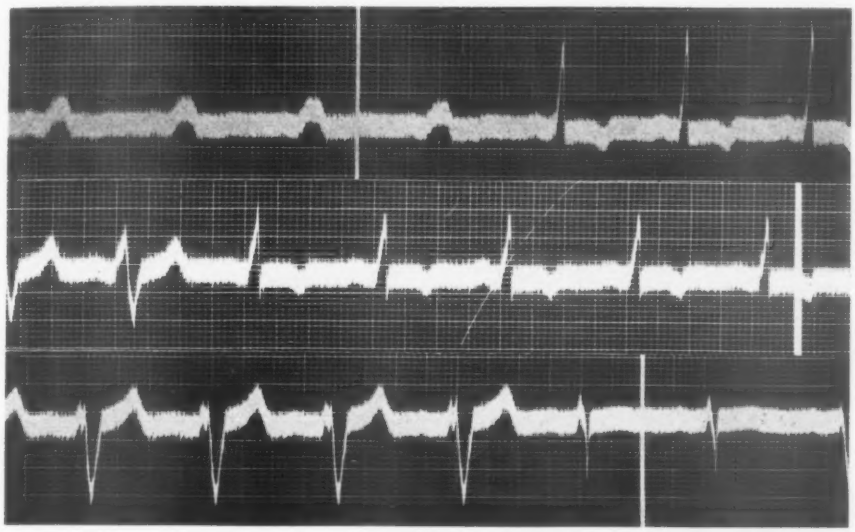


Fig. 2.—Case 2. Leads I, II and III with respiratory tests, vertical white signal lines marking beginning and end of deep inspiration. In all Leads reproduced, only the end is signalled.

plexes. After only slight exertion and by the application of the respiratory test complete transition from the bundle-branch QRS interval to the normal was recorded in all three leads, as the heart rate remained practically unchanged at 75 beats per minute.

The bundle-branch block was relieved by rest in bed, and it recurred with the slightest exertion. The patient was discharged, with directions to take theophylline ethylenediamine regularly, and digitalis when necessary under the direction of a physician. On March 15, 1930, she was still living and had about the same symptoms which she had had on admission. She was advised to return to the hospital for further study.

CASE 3.—Mrs. L. H., aged 37 years, a married, white housewife, came to Charity Hospital October 8, 1928, complaining of weakness. The trouble had begun several weeks before the patient entered the hospital and shortly after her marriage. She began feeling tired and was sometimes conscious that her heart beat too rapidly. Previous to this she had always been strong and able to do housework without

any difficulty. She had had measles and mumps as a child and influenza in 1918. One attack of sore throat occurred eight weeks before admission. It had been considered mild, but it was probably a serious streptococcic invasion. The patient had not menstruated for two months.

*Physical Examination.*—The patient was distinctly pale and weak but apparently not in pain. Her eyes were held closed, and her nose was pinched and her facies strained. The pupils were equal and reacted to light and in accommodation. The ears were normal and the teeth in good condition. The tongue was coated with a gray white fur. The tonsils were largely submerged and showed signs of previous inflammation. There was, however, no evidence of an acute infection. Along the great vessels of the neck were conspicuous pulsations of a bounding, throbbing character synchronous with the heart beat. The chest was symmetrical, and expansion was fairly good and was equal on the two sides. No râles or suppression of breath sounds was noted. The apex impulse was not seen but could be felt over all the precordium. There were no thrills. A fairly loud, rough, blowing systolic murmur was heard best over the apex impulse and transmitted downward to the left and upward over the precordium to a less degree. The first sound was entirely replaced by a murmur. There was also a splitting of the first sound resembling closely a late diastolic murmur, rumbling in character. The systolic murmur was also heard at the aortic area, but later a high-pitched long diastolic aortic murmur became conspicuous. These murmurs could also be heard over the great vessels of the neck. Later a to-and-fro friction rub developed and persisted.

The abdomen was of normal contour and no masses were felt. On deep pressure in the left iliac fossa slight tenderness was found. The patient had a persistent fever. Electrocardiograms showed a complete bundle-branch block of the His bundle type. The blood count revealed a secondary anemia and a leucocytosis. The urine on October 8, 1928, showed many red cells and some pus cells, while a catheterized specimen on October 15, showed a trace of albumin, pus cells in masses and also occasional red blood cells. On October 23 there was only an occasional pus cell found, and on October 30 the urine was negative. There was a 40 per cent excretion of phthalein in two hours on October 22.

The vaginal examination revealed signs of an early pregnancy. The external os was plugged with secretion. The uterus was in a normal position and was freely moveable. The tubes were not enlarged, though they were slightly tender. The interruption of the pregnancy was considered but advised against because of the presence of an acute endocarditis probably of rheumatic origin and of the bundle-branch block. It was decided to tide her along and carefully observe her progress.

The blood pressure varied somewhat during the course of pregnancy, from 120/80 to 100/50. X-ray examination (October 26) showed the heart shadow normal with no evidence of dilatation of the aorta. The lung field appeared quite clear. The Wassermann test was negative on October 10. The feces examination on April 12, 1929, was negative for ova and parasites. A blood culture taken on October 23, 1928, showed a staphylococcus aureus in seventy-two hours with one colony per cubic centimeter of blood. A blood culture taken on November 28, 1928, showed no growth in seventy-two hours.

*Progress.*—The condition of the patient became worse during the first hospitalization. She began bleeding from the nose on October 24, 1928, and this condition recurred several times. On November 9, 1928, she complained of pain in the epigastrium and also in the left hypochondriac region. This pain was relieved by pressure. The symptoms of the acute endocardial infection subsided without definite signs of embolism, but the block persisted. She was an ardent Catholic opposed to abortion and very desirous of having a baby. Because of these facts and especially because of the persistence of the bundle-branch block she was allowed to continue in the pregnancy and to go home for a few months beginning January 6, 1929.

On returning to the hospital for the second time, March 10, the patient complained of palpitation and dizziness, particularly marked after exertion. The bundle-branch block, however, persisted as did also the signs of valvular heart disease, but no fever was present, nor were there any signs of acute endocardial infection. The electrocardiographic studies showed a persistence of the complete bundle-branch block in all curves taken before April 20. On this date a curve taken showed normal intraventricular conduction, but the bundle-branch block appeared again on April 30. She was observed daily up to the seventh and a half month of pregnancy when it was found after she had had good rest in bed that she actually had transient periods of normal conduction.

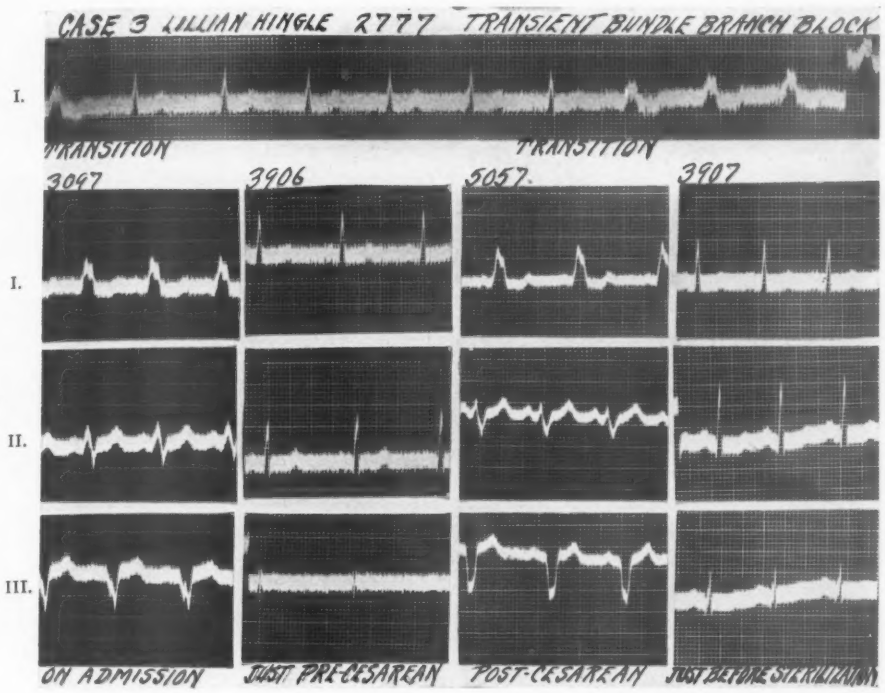


Fig. 3.—Case 3. Above, transition in Lead I. Below from left to right, the three Leads on admission, just before and just after the cesarean section, and just before sterilization.

Cesarean section was decided upon and was done during one of these periods of normal intraventricular conduction, on May 4, by Dr. E. L. King under local anesthesia and ethylene. A living baby was delivered. Bundle-branch block reappeared promptly postoperatively. Five days after Cesarean section, on May 9, normal conduction had returned, and the blood pressure was 106/48. The sterilization procedures which had been postponed were accomplished in a later period of normal intraventricular conduction. The patient was discharged from the hospital in fairly good condition.

*The electrocardiograms* (Fig. 3) show in the top strip the transition from bundle-branch block with a short, blunt, broad, slurred QRS complex measuring 0.14 second to a sharp narrow QRS of 0.06 interval for six beats and then another abrupt shift to the bundle-branch block. The P-R intervals are about 0.04 second longer during the period of conduction than they are during the block. The other

sets of curves, however, show greater differences in the intervals. Electrocardiogram #3097 shows intraventricular block with a rate of 100; #3906 conduction at 88; #5057 IV blocked at 91 and #3907 conduction at a rate of 90 per minute.

### SOME OTHER INSTANCES OF CHANGES IN INTRAVENTRICULAR CONDUCTION

Besides the three special cases, in which by respiratory maneuvers it was possible to produce short periods of normal intraventricular conduction abruptly following a period of bundle-branch block, we have five other cases of high grades of partial bundle-branch block. In these, in the presence of partial or almost complete bundle-branch block or of defective intraventricular conduction with or without other mechanism or rhythm disturbances, there appeared at times normal short QRS intervals. Usually in the presence of an irregularity, after the longer rest periods and recovery from fatigue there occasionally appeared isolated or repeated complexes with intraventricular intervals of 0.08 second or less. These complexes almost invariably followed the longer pauses. Only two notable exceptions occurred in cases, not included in this series, with free aortic regurgitation in which the longer the pause the greater was the subsequent QRS interval and aberration. This paradoxical finding is possibly to be accounted for by the continuation of the regurgitant stream during diastole mechanically stretching the ventricular wall and interfering with the propagation of the impulse. The improved conduction is thus usually the result of the longer rest period of the fatigued tissue which allows more time for the removal of waste metabolic products as well as for the completion of anabolic processes which are probably slower in the conduction tissues which have an impaired circulation. This rate change is often, though not always, an important factor. One patient had several paroxysms of tachycardia in some of which there was normal conduction in others bundle block.

In these cases the prognosis seems to be better than in those in which the complete block has persisted, but not quite so good as in the cases in which periods of normal conduction can be secured, by rest or other means. The fact that the conduction system can occasionally yield normal appearing complexes after slightly longer rest periods indicates that fatigue plays an important part in the conduction disturbances and that rest with resulting improved intracardiac circulation, oxygenation, nutrition and elimination offers the possibility of restoration of normal function.

CASE 4.—G. A., a white laborer, aged 60 years, came into the hospital March 26, 1929, because of shortness of breath and rather rapid heart action. His symptoms had begun about four or five months previously when he first began to be troubled by attacks of rapid heart action during which he was conscious of every heart beat. The attacks appeared more frequently as time went on and were accompanied by severe "weak spells." A cough had been present for several months, and dyspnea had been noticed on exertion. About a month before admission he had become definitely orthopneic, and had been unable to lie in bed.

His feet and ankles showed some puffiness which gradually increased until easily recognizable edema was present, increasing until it was above the knees.

The family history was irrelevant, but in his past history he had had several infectious diseases which might have contributed to the heart disease. At about the age of fifteen years he had a severe attack of diphtheria which was not treated with antitoxin. He had had a mild typhoid infection. He denied venereal disease as a possible etiological factor. He had suffered a severe attack of influenza during the epidemic of 1918 and again in 1929. The latter seemingly precipitated his trouble.

The *physical examination* showed an extremely orthopneic white male, of sthenic habitus, measuring about 69 inches, and weighing about 180 pounds. Even in

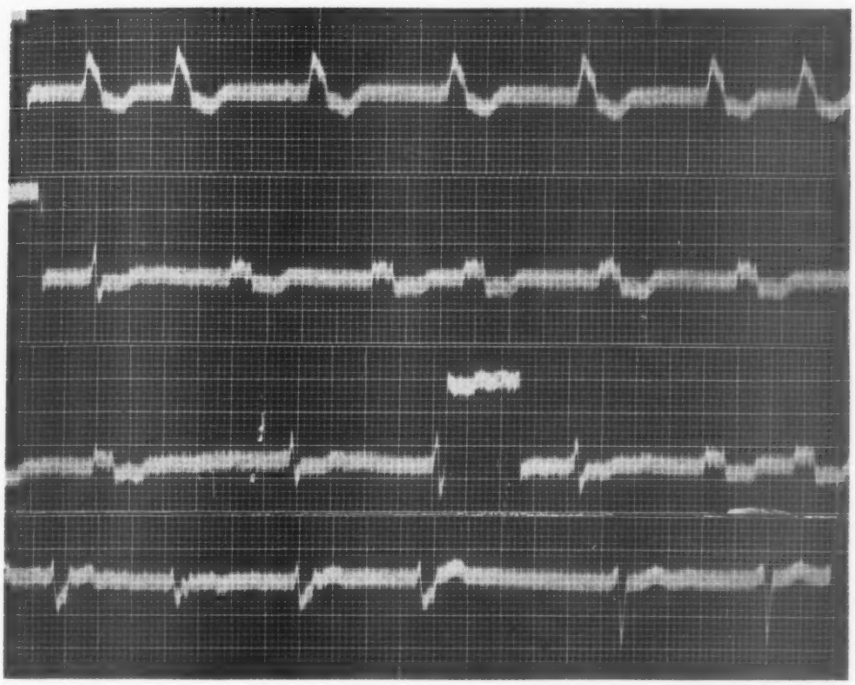


Fig. 4.—Case 4. Leads from above downward, I, II, III, showing broad and narrow QRS complexes of varying degrees of intraventricular conduction disturbance. At times the patient showed complete bundle-branch block with flutter; at other times there were normal conduction and flutter.

his propped-up position in bed he was distinctly dyspneic. The pupils reacted to light and in accommodation. The neck veins were engorged, and there was some systolic pulsation present in them. The maximum apex impulse was in the sixth interspace 14 centimeters from the midsternal line. Pulsations were regular and rapid. The retromanubrial dullness measured 5.5 centimeters. The cardiac outline extended 3 centimeters to the right and 14 centimeters to the left. A blowing, systolic murmur was heard in the mitral area. The pulse was full and bounding; at times it was 124 per minute and the rhythm was regular, at other times it was only 80 and definitely irregular, caused apparently by premature contractions. No pulse deficit was made out. The arteries were moderately sclerosed and large. The systolic blood pressure was 118 millimeters of mercury, and the diastolic was

92 mm. There were dullness at the lung bases posteriorly and crepitant râles throughout the basal area. Edema was present in the lower extremities and up about the knees.

The urine showed specific gravity of 1.010, albumin, no sugar and occasional hyalin casts. The P. S. P. excretion was 20 per cent in two hours. The Wassermann test was negative. The blood chemistry showed an NPN of 57 mg., creatinine 2, uric acid 5, and blood sugar 74 mg. per 100 c.c.

*Electrocardiograms* (Fig. 4) taken on admission, March 26, 1929, showed an auricular tachycardia of 134 per minute and a QRS interval of 0.06 second. The same disturbance was present on the following day and on April 6 there was a drop in rate to 120 to 100 and distinct evidence of defective intraventricular conduction, with a QRS interval of 0.12 second and a P-R and a suggestion of impure flutter rather than paroxysmal tachycardia. There were changes in T-waves, short paroxysms of rapid rhythm and an irregularity resembling two-to-one and three- or four-to-one block. Curves taken the next day showed an intraventricular conduction defect with regular rapid rhythm. The apparently complete bundle-branch block complexes were short, blunt and broad, simulating those of arborization block. The same condition was present on May 24, intraventricular block being of the ordinary type. On July 8 there was a return to the normal narrow ventricular complexes measuring 0.06 second with a presence of the auricular tachycardia persisting. The same conditions were found on July 11. On July 30 the electrocardiograms presented a bundle-branch block of the ordinary type with a QRS and a P-R interval of 0.16 second. Frequently ventricular and auricular ectopic beats were seen. In another day the complexes were distinctly blunt and shorter. Four days later these slight changes were still present. After treatment in the hospital for a month the electrocardiograms on August 30 showed perfectly normal ventricular complexes with a QRS interval of 0.06 and slightly defective auriculoventricular conduction time with an increase of P-R interval to 0.26 second and occasional blocking. The next day two-to-one block had developed, while the changes in the T-waves were more marked. Occasional ventricular ectopic beats or premature contractions appeared. The patient was discharged from the hospital considerably improved and remained in the Convalescent Home for a short time. On December 30 he was brought into the hospital *in extremis* with congestive failure and died the same day. The diagnosis had been arteriosclerotic and chronic nephritic heart disease with congestive failure apparently precipitated by influenza, attacks of paroxysmal tachycardia and bundle-branch block.

CASE 5.—M. J., a Syrian, aged 65 years, came into the Charity Hospital July 27, 1929, complaining of swelling of the feet and shortness of breath. Symptoms had been present since an attack of influenza four months previously. In this illness he had been confined to his bed for two months with chills and fever. He seemed to have been relieved somewhat by remaining in bed, but he still had palpitation and slight pain in the region of the heart. These troubled him especially after the eating of a heavy meal. Occasionally he was nauseated and vomited a greenish material. Nocturia disturbed each night's sleep four or five times. Swelling of the feet had been present for about three months, and had been quite severe at times when he attempted to get up and remain out of bed. He was totally incapacitated. He had taken only small amounts of digitalis as his only treatment. He had had no serious illness in the past. Two of his children were living, and four had died of unknown causes. His father had dropped dead, and his mother had probably died of heart disease for she had suffered from dyspnea and pain in the heart.

On *physical examination* the old man was found to be of sthenic habitus, 64 inches tall, and to weigh 122 pounds with very little panniculus. He was lying on his back apparently comfortable, exhibiting no dyspnea or cyanosis. The pupils reacted properly; all of his teeth were missing, no snags were present; the thyroid

and other neck glands were not abnormal; the neck veins and arteries presented no abnormal pulsation and nothing that was strikingly unusual; the apex impulse was not felt and could not be seen. No thrills or shocks were palpable. The cardiac retromanubrial dullness measured about 5.5 centimeters. The general cardiac dullness extended 2 centimeters to the right and 10 centimeters to the left of the midsternal line. The heart was slow and slightly irregular. The sounds, obscured by the conspicuous emphysema of the chest, were distant, and no definite murmurs could be made out. The arteries were slightly thickened; the blood pressure was 105 mm. Hg., systolic and 70 diastolic. Aside from emphysema the lungs presented nothing abnormal. The vital capacity was 2,000 cubic centimeters.

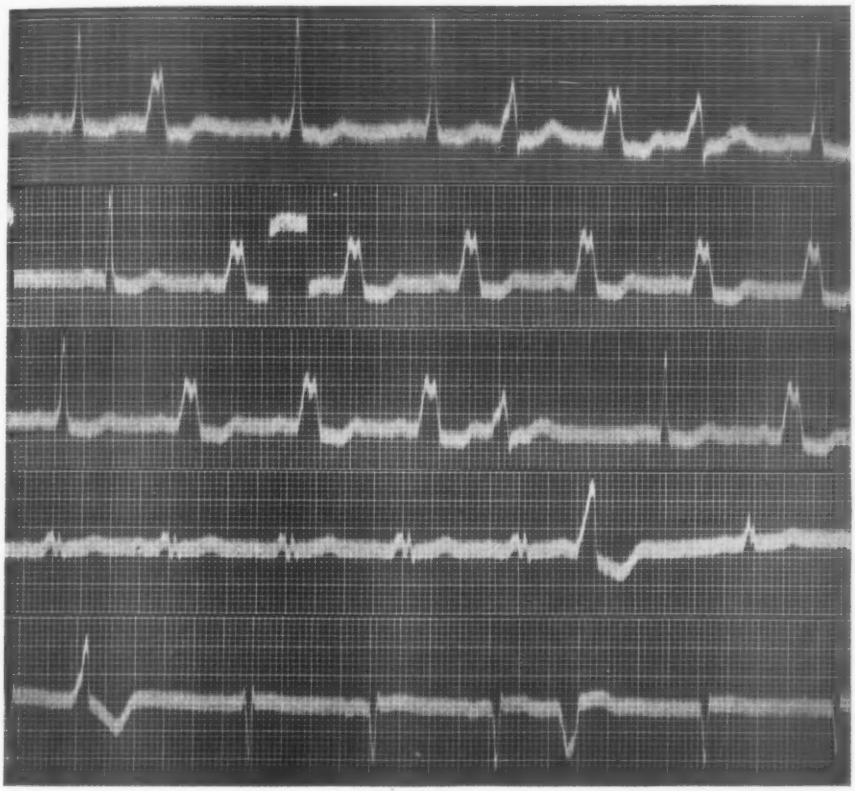


Fig. 5.—Case 5. From above downward, Leads I, I, I, II, III, (see text).

The abdomen was somewhat distended, no areas of tenderness were felt. The liver border was not felt, nor was the spleen abnormally large, and no ascites was present. The feet and legs showed a distinct edema. The urine was negative except for the presence of pus cells. The specific gravity was 1.010. The P. S. P. excretion was 30 per cent in two hours. The nonprotein nitrogen was 33.3 mg. per 100 cubic centimeters of blood; the urea nitrogen was 16.7 mg.; the creatinine 1.3 mg.; the uric acid 2 mg. and the blood sugar 93 mg. per 100 cubic centimeters of blood. The Wassermann test was not made.

*Electrocardiograms* (Fig. 5) taken on admission showed auricular fibrillation; QRS intervals of 0.08 second somewhat like Robinson's Case 5, with slightly slurred up-strokes of R-1 and downwardly directed main deflections in Lead III. Occa-

sional ectopic beats were present; here and there one was preceded by a clear cut P-wave suggesting a supraventricular origin with intraventricular block due to the persistence of fatigue as brought out by the prematurity. T-waves were negative to a great extent, and in Lead I and II there was a slight S-T segment shift from the iso-electric line. The electrocardiograms taken the next day showed the ventricular complexes preceded by P-waves to be predominating, and the more normal appearing complexes of a QRS of 0.07 second occurred only after long post-extrasystolic pauses. There predominated ventricular complexes of the ordinary bundle-branch block type, with the QRS measuring 0.16 second, a deep notching at the top and diphasically directed T-waves. Respiratory maneuvers apparently had little effect on the bundle-branch block. With complete rest in bed there was a return to normal appearing complexes. The patient was discharged distinctly improved and has been lost track of. He has not yet responded to the follow-up card.

CASE 6.—Mrs. E. P., housewife, white, aged 62 years, was admitted to Charity Hospital October 12, 1928 because of dizziness and pain in the heart, swelling of the abdomen and feet. The symptoms had been present for about three months and apparently had been precipitated by an acute respiratory infection. Cough had troubled her, with expectoration moderately free. She often vomited and felt nauseated after an attack of coughing. Her sleep has been disturbed as often as twelve times by nocturia with, however, the production of only small amounts of urine. Ankles and abdomen had become swollen shortly after the onset of the respiratory infection and cough. Palpitation and shortness of breath had been noted upon slight exertion and later even on eating and drinking. Dizziness and pain in the precordium region were noticed by the patient whenever she turned on her left side in bed. She had not been able to do any work for several weeks.

The *physical examination* revealed a white, French woman, 66 inches in height, weighing 160 pounds, of sthenic habitus, in a state of poor general nutrition, distinctly breathless even in a sitting position. Pterygia were present in both eyes; the pupils were contracted but reacted to light. There were many missing teeth and several infected snags remained.

The apex impulse was felt in the fifth interspace, 12.5 centimeters to the left of the midsternal line. The aortic arch was not palpable in the supersternal notch; no abnormal pulsations were seen. The retromanubrial dullness measured 5.5 centimeters, and the area extended 3 centimeters to the right and 14 centimeters to the left of the midsternal line. The heart was rapid, 128 per minute. Numerous runs of rapid rhythm with premature beats were noted. The first sound at the apex was abrupt and prolonged; the second sound at the base, reduplicated. The pulse was small, soft, rapid, and there was a distinct deficit of about 36 beats between apex and radial. Blood pressure was systolic 130, and the diastolic was 94 millimeters of mercury. The peripheral arteries were not definitely sclerosed. Definite râles were found at both lung bases posteriorly. The lungs were somewhat distended and emphysematous.

The abdomen was greatly distended by a marked ascites. A distinctly sharp edge of an enlarged liver was found. There was slight edema of the extremities.

Urine showed 1.020 specific gravity, contained 3 per cent albumin, no sugar and no casts, and only a few pus cells. The Wassermann reaction was negative.

*Electrocardiograms* (Fig. 6) taken on October 12 showed a high grade of auricular fibrillation, short, blunt, broad complexes with defective intraventricular conduction. The QRS intervals measuring about 0.12 to 0.14 second. Occasional premature contractions with a QRS of 0.8 second were seen. The curves of the following day were quite similar. After three days' rest in bed the complexes were not so blunt, and the QRS intervals measured 0.06 to 0.08 second, the rhythm was

quite regular except for occasional ectopic beats. No definite P-waves were seen. On March 16, 1929, there was a return to the broad complexes in some parts of the curves taken. The QRS intervals increased from 0.08 second to 0.14 second. The interval length for the most part varied irregularly with occasional ectopic beats and occasional short paroxysms of regular rhythm which was apparently of nodal or junctional origin. On March 17 the rate was very much reduced, no paroxysms were photographed, and on March 19 conditions were about the same. On December 6 there was little change except that the complexes were getting

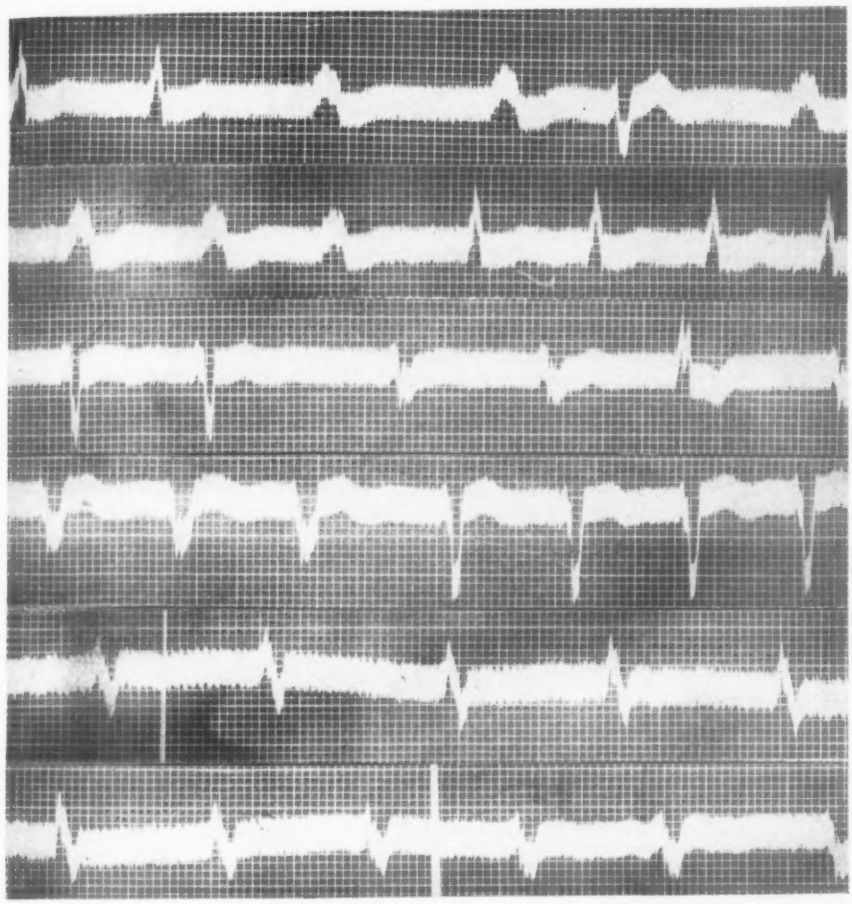


Fig. 6.—Case 6. Leads from above downward, I, I, II, II, III, III. Deep inspiration signalled.

shorter and more blunt. This was especially marked in the very low, broad, blunt complexes of March 5, 6, 7. Bizarre complexes were frequently seen among the many premature contractions. The patient failed to improve much but was discharged and died about one week after her return home.

CASE 7.—P. S., a white decorator, aged 66 years, entered the hospital on April 11, 1930, because of shortness of breath and palpitation. The onset of these symptoms dated back to two and a half years before his entrance into the hospital. Swelling of the ankles and abdomen began about this same time. All symptoms disappeared during the night and were banished for several weeks after a period

of rest in bed even without medication. One year after the onset, treatment with digitalis was started and continued irregularly from that time for the next year and a half. Frequent periods of rest in bed were necessary.

The family history revealed the facts that the patient's mother had died at 63 years of "heart trouble" and his father of "dropsy" at the age of 53 years. The patient had had mumps as a child and pneumonia at the age of twelve. Gonorrhea contracted at the age of 25 completed the list of past diseases. He was married at 21 years and was the father of 12 children of whom there were 7 living and well. There had been no miscarriages.

The *physical examination* showed an hypersthenic individual weighing about 150 pounds and measuring about 64 inches. The pupils reacted to light and in accommodation. The tonsils were small and red. His teeth showed pyorrhea and some caries. The aortic arch was barely palpable in the suprasternal notch, but there was evidence of dilatation of the aorta. The apex beat was in the fifth interspace outside the left midclavicular line. The heart rate was 50 and the

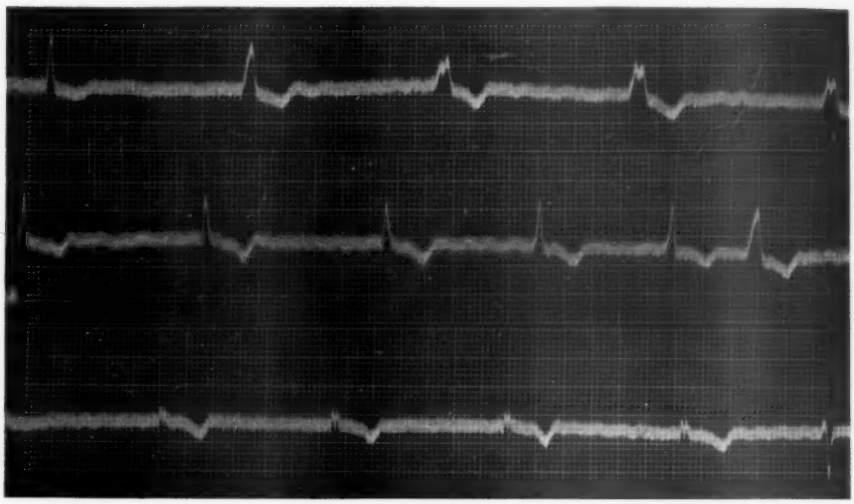


Fig. 7.—Case 7. Auricular fibrillation with changing intraventricular conduction time especially in Lead I.

rhythm irregular with many premature contractions. There was a soft right basal systolic and a very soft apical systolic murmur just within the nipple line. The arteries showed moderate arteriosclerosis. The blood pressure was systolic 120 millimeters of mercury and diastolic 90. There were moist râles at the bases of the lungs. The abdomen was full and soft.

The urine showed a specific gravity of 1.013 and was negative except for the presence of many hyaline and granular casts. The P. S. P. excretion was 45 per cent. The Wassermann test was negative. The blood chemistry showed nonprotein nitrogen 44.4; urea nitrogen 23; creatinine 1.42; uric acid 4.44; and blood sugar 108 mg. per 100 cubic centimeters. The hemoglobin was 80 per cent, the red blood cells numbered 3,281,000 and the white blood cells 4,000 per cubic millimeter. The differential count showed: small mononuclears 26; large mononuclears 6; and neutrophilic polymorphonuclear cells 68.

The first electrocardiogram (Fig. 7) taken April 16 showed auricular fibrillation, left ventricular predominance, questionable defective intraventricular conduction with a QRS of from 0.06 to 0.08 second. The heart rate was slow, 56 beats per

minute. There were occasional ventricular premature contractions as presented in complex 4 of Lead I. After complex 5 (Lead I) there is a probable shift to an idioventricular pacemaker with an increase of the QRS to 0.12 and 0.14 sec. in the last four complexes. In Lead III after a narrow 0.08 second QRS complex with upright T-waves there are four blunt, broad 0.10 second QRS complexes with negative T-waves. On April 17 there was less conspicuous transient defective intraventricular conduction along with auricular fibrillation with the rate increased about 10 beats per minute. The QRS was 0.08 to 0.10, and the rate was 60. On April 21 the rate was 74 with auricular fibrillation and more frequent ventricular ectopic beats or aberration, and the QRS, 0.09. T-1, T-2 and T-3 were negative. On April 22 the rate was 78 and the QRS 0.09 to 0.12 and sometimes

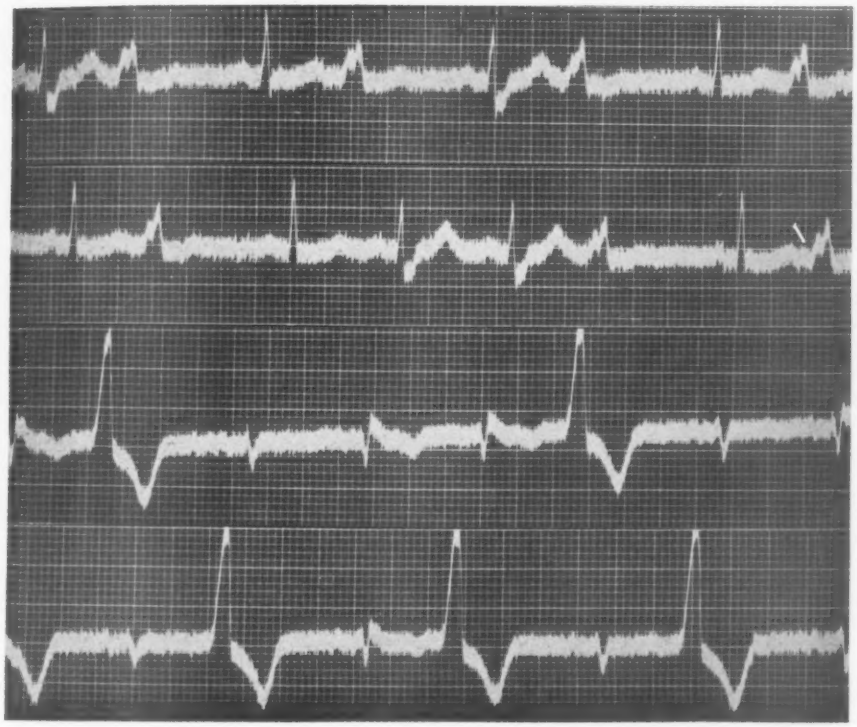


Fig. 8.—Case 8. Leads, from above downward, I, I, III, III. Note abrupt changes in QRS width in complexes following compensatory pauses.

broader complexes and greater aberration after longer rests. On April 26 the rate was 88 and the QRS 0.08 and there were rarely broad complexes with aberration. Auricular fibrillation persisted, and on June 14 with a rate of 110 to 120 the QRS measured never more than 0.08 second. Left ventricular predominance with a rise of the S-wave on deep inspiration and negative T-1, T-2 and positive T-3 were present, but no broad and bizarre complexes appeared.

He was given digitalis again along with theophylline ethylenediamine and a low-protein, salt-poor diet on which he improved considerably. After the patient was discharged from the hospital on April 22 edema recurred, and he returned to the out-patient clinic where he responded to the digitalis, squills and mercury pill, and normal sinus mechanism was established. He was in regular follow-up attendance until December 15, 1930, when he died suddenly.

CASE 8.—Mrs. M. A., a white housewife, aged 57 years, came into the Heart Station of Charity Hospital June 10, complaining of shortness of breath, palpitation, dizziness, pain in the left arm and swelling of the feet and ankles. The symptoms had come on insidiously, and dyspnea had become noticeable two years before admission. The vertigo was troublesome for three months and the pain for six weeks, previous to the time she presented herself for treatment. Paroxysms of dyspnea and palpitation were noted even at rest at times, but always on exertion. The pain in the left arm was precipitated by effort and excitement and extended from the shoulder to the elbow. It had been sharp at times but was for the most part dull and of short duration. She had never had an attack of syncope but had felt weak and faint at times.

The *physical examination* revealed an obese middle-aged woman of sthenic habitus moderately orthopneic at times and with a slight tinge of cyanosis. The teeth had all been removed. The thyroid isthmus was slightly enlarged. The heart apex impulse was felt in the fifth interspace 10 centimeters to the left of the midsternal line; the aortic arch was not palpable in the suprasternal notch. The cardiac dullness extended 3 centimeters to the right and 12 centimeters to the left of the midsternal line. The teleroentgenogram showed an arch of 4.6 centimeters with a transverse and longitudinal diameter of 16 centimeters each. The heart rhythm was irregular with premature contractions appearing regularly after every other or every fourth beat at times. The aortic second sound was accentuated. No significant murmurs were heard. The blood pressure was 162 mg. Hg. systolic and 88 diastolic. The peripheral arteries were not appreciably abnormal for the patient's age. The lungs were negative. There were only a slight tenderness in the liver region and a questionable edema of the ankles.

The urine was of 1.010 specific gravity and contained no albumin or sugar or casts but a few pus cells. The nonprotein nitrogen was 33.3 mg. and the blood sugar 78 mg. per 100 c.c. of blood. The blood Wassermann test was negative.

The *electrocardiograms* (Fig. 8) showed frequent ventricular premature contractions producing a bigeminy most of the time. A closer study of the narrower supraventricular complexes revealed distinct changes in the QRS width and especially the breadth of the S-waves. After the longer postextrasystolic pauses the QRS interval measured about 0.07 second, while after the shorter pauses the QRS interval increased to 0.10 second and when the rate was increased, abolishing the ectopic beats and compensatory pauses, the QRS interval broadened to 0.12 second. In Lead II this state of affairs was present throughout. In Lead III the changes were less readily observed but were nevertheless clearly present. The findings suggested a degree of partial, perhaps incomplete, bundle-branch block in which the conduction was at a critical level such that slight changes in rate and the length of the rest period were sufficient to cause sudden and pronounced changes in the intraventricular conduction time. This change was sudden, of an all-or-none character, and the partial intraventricular disturbance, even though slight, was of Type II of partial intraventricular block.

## THEORETICAL DISCUSSION

A consideration of certain physiological matters is essential adequately to present our point of view concerning the mechanism of partial bundle-branch block as the intraventricular counterpart of partial A-V block. It will be necessary for the sake of orientation to discuss in detail the theory of A-V block.

Much evidence has accumulated which indicates unmistakably that the fundamental phenomena of conduction are everywhere the same,

in nerve, in skeletal muscle, and in cardiac muscle, whether the latter be a part of the auriculo-ventricular junction, the auricular muscle, the ventricular muscle, or the Purkinje fibers. This view is now widely accepted, although there are those who still cling to an opposing conception, at least so far as the A-V junction is concerned (Mobitz,[12] 1924, 1928; Straub and Kleemann,[26] 1917). The clinical cases herein reported afford an opportunity of discussing certain matters which have up to the present not received adequate attention, or emphasis and which are still not generally understood.

### *Auriculo-Ventricular Block*

Wenckebach has recognized and described two main kinds of A-V block, named by Mobitz[12b] Type I and Type II. Each, of course, may appear in variously modified form. But, for clarity in discussion, we shall briefly characterize the essential features of each. The first type is the one ordinarily regarded as typical of heart-block, showing as it does the occasional or more frequent dropped ventricular beats; the comparatively rapid, often apparently normal, conduction of the following auricular impulse; and the more or less gradual prolongation of subsequent P-R intervals until an impulse fails to reach the ventricle and another beat is dropped producing "Wenckebach's periods." In the severer stages of this type, we observe 2:1 or more rarely the higher grades of block or complete block.

This type of block is now comparatively well understood. An explanation similar to that offered by us has been adapted to the various sub-types of block in an interesting paper by Scherf.[13] Wenckebach and Winterberg's[14] conception of the mechanism of Type I block is much the same. Beginning with the dropped beat, the explanation previously advanced by us is this. The auricular impulse that is to be blocked penetrates the junction to a given depth and is blocked at a transverse plane, *B*. Because it is blocked, the tissue distal to plane *B*, not having responded, has extra time for recovery. The next impulse from the sinus consequently finds the region *C*, immediately beyond *B*, responsive and is, therefore, transmitted to the ventricle. The third impulse finds *C* depressed because of its previous response, and is transmitted more slowly. The fourth impulse finds *C* still more depressed, either because of cumulative fatigue or for some other reason, and consequently either fails to cause a response of *C*, or is transmitted still more slowly. Sooner or later unless the factors leading to recovery of *C* balance those responsible for its depression, another impulse must fail to reach the ventricle. In the most stable form of partial block, 2:1, *C* is capable of responding only to every other impulse.

The less common and less understood variety of A-V block is Type II. It would be premature to attempt to explain it, but we may examine its outstanding characteristics. First observed by Wenckebach[15] and by Hay[16] Type II block shows no change in the length of

the A-V interval at the time of transition from one stage of block to another. The A-V intervals remain constant throughout, and, in perhaps the majority of cases, within normal limits. Although protean in its manifestations, it is in cases of block of Type II that we commonly see abrupt transitions from apparently normal conduction to temporary complete block or the reverse; or two or more successive transmissions of the auricular impulse to the ventricle followed by two or more successive failures, these occurring in irregular sequence. A good example of the latter is illustrated by Mobitz.[12] Abrupt transition from an apparently normal mechanism to complete block is well shown in Case 4 of Wilson and Herrmann[21] and by Ashman and Herrmann.[17] This is the form of block which finds its counterpart in intraventricular conduction in the cases herein discussed, where there is abrupt transition from seemingly complete bundle-branch block to normal intraventricular conduction or the reverse. Whether or not the latter block was actually complete is, perhaps, questionable, as will be mentioned below.

Scherf[13] has made the interesting suggestion that in A-V block of Type II, when the conduction time for impulses passing to the ventricles is within normal limits, the damaged or depressed area in the conducting pathway is practically limited to a plane cutting transversely across the A-V node or bundle. Thus, when the impulse does cross the extremely narrow gap, the loss of time is negligible. This explanation is in complete harmony with the converse conception which Herrmann and Ashman[18] had expressed to account for the phenominally long conduction times, ranging up to 1.01 second in one of their cases, namely, that a very long A-V interval is the result of a great breadth of injured or depressed tissue through which the impulse must make its way. They also stated that a shorter conduction time, other things being equal, argued for a shorter stretch of depressed tissue in the conducting pathway.

### *Intraventricular Block*

We are now in a position to inquire whether, in intraventricular block, we may recognize the counterparts of Type I and of Type II A-V block. One of the chief problems which confronts us is to explain why a sequence of events similar to those observed in partial A-V block of Type I with "dropped beats," has never been observed in the human case. We cannot look for the answer in a fundamental difference between the physiological properties of the bundle or bundle-branch tissue, and the A-V junction as Mobitz[12a] believed, but rather in the differences in the anatomical relationships and conditions. Substantiation of this view is found in experiments of Scherf and Shookhoff.[19] After cutting the left bundle-branch and temporarily compressing the right, regular Wenckebach periods, i.e., typical 3:2, 4:3 grades of heart-block, were recorded. In discussing the rea-

sons for the rarity of partial bundle-branch block, and the absence of reports of bundle-branch block of the 4:3, or 3:2 type, we must briefly consider the various possibilities. As a first stage in block, there may be slight or moderate delay in one bundle-branch, a delay of from 0.005 to about 0.04 second. Such delay results in the well-known electrocardiographic picture of incomplete bundle-branch block. In the next stage the prolongation of intraventricular conduction time may be greater. Here the impulse, sweeping normally through the opposite ventricle, penetrates the septum and activates the ventricle whose bundle-branch is damaged before that ventricle can be reached by the impulse delayed in its own branch. When, and if, this latter impulse does reach its ventricle, the tissue is refractory. The electrocardiographic picture is that of complete bundle-branch block. To quote a recent paper by Slater[10] "innumerable cases which are called complete bundle-branch block are in reality incomplete bundle-branch block." And further, according to Slater, "there is a matter of only 0.035 to 0.05 second for the play of the various types of incomplete bundle-branch block to make itself manifest." "This latter fact," he says, "is what has made it so hard to find clinical examples of the various types of block to correspond to those of the A-V block."

Let us apply this conception to a hypothetical 4:3 bundle-branch block, of Type I which, but for the reason Slater gives, would resemble typical 4:3 A-V block. The first impulse will pass the defective bundle-branch with little or no delay. Thus, the ventricular complex is of practically normal form. The next impulse, however, to judge from analogy with A-V conduction, is considerably delayed. The corresponding complex is, therefore, typical of those of complete bundle-branch block. And the same thing will be true of the next two complexes, in which the delay is even greater. The fifth impulse, however, goes through, and again we should expect to see a complex of relatively normal configuration. The result will be an electrocardiogram in which every fourth QRS is relatively narrow, the others broad. This is precisely the type of electrocardiogram Slater publishes. His figure may, therefore, represent 4:3, 3:2 partial block of Type I. On the other hand, great progressive prolongation of the P-R intervals in partial heart-block with dropped beats is not always seen. And experimentally all degrees of prolongation of conduction time are seen in compression block, from those in which block occurs with hardly measurable variations in the intervals to those in which the prolongation and variation is extreme (Ashman, unpublished observations). Therefore, unless there be some explanation other than that of Slater, it is hard to understand why the type of block under discussion is not sometimes observed.

But let us carry our analysis still further. After 4:3 and 3:2 partial A-V block of Type I, we find 2:1 block, which as Wenckebach and Winterberg[14] point out cannot be identified as to type, unless it is known

that the same heart at other times presents the typical picture of one or the other type of intraventricular block. Leinbach and White[9] have reported a very clear example of 2:1 partial bundle-branch block and one from Stenström,[27] and other illustrations are to be found in Wenckebach and Winterberg.[14] It is impossible, of course, to say whether they are of Type I or Type II.

It is generally stated, and there is no reason to question the statement, that 3:1 block is the stage following 2:1 A-V block of Type I. That it is rarely seen is a consequence of idioventricular activity. The ventricle rarely waits for the third impulse to come through, but escapes and thus the electrocardiographic picture of complete heart-block is seen. In the bundle branch, however, if the arguments of Slater tell the whole story, there is no apparent reason why partial 2:1, 3:1, 4:1 or even higher grades of block should not be seen relatively frequently. The electrocardiogram, of course, should show more or less frequent, relatively normal, ventricular complexes, each pair separated by one, two or more complete bundle-branch block complexes. It is manifestly impossible to prove that Slater's case does not represent just such a mechanism, i.e., 3:1, 4:1 block of Type I.

At the same time, however, a third possibility exists. Slater's electrocardiograms may, as he himself believes, portray a 3:1, 4:1 block of Type II. But it is quite impossible to decide with certainty between these three explanations.

It should now be evident from our discussion that the arguments advanced by Slater do not satisfactorily explain why partial bundle-branch block, demonstrably of either type, is such a rarity. The physiologically satisfactory answer is given by Wilson and Herrmann.[20] In contrast to the situation in partial A-V block, the region of local depression in bundle-branch block is reached from both sides by the impulse, first through the branch from above and a little later from below by the impulse from the opposite ventricle. The consequence is that every impulse finds the physiological state of the depressed region the same. Excepting under unusual circumstances, therefore, there is no possibility of variation in the behavior of that region, or, in other words, of the appearance of partial block. Partial block of Type I can only appear, as we have pointed out, when some part of the conducting pathway periodically fails to respond and, therefore, gains additional time for rest and recovery. Appreciation of this point of view will enable one to see that the other arguments to explain the rarity of partial bundle-branch block are superfluous.

However, physiological states and structural relationships of depressed and nondepressed segments of the bundle branch can be imagined which could lead to the appearance of partial block of Type I. For example, a condition of irreciprocal conduction or unidirectional block may be present. Ashman and Hafkesbring, using ven-

tricular strips from the turtle heart, demonstrated that an impulse may pass a depressed region, if it travels first through normal, then enters strongly depressed, then slightly depressed and then reenters normal muscle. But if the impulse was required to travel in the opposite direction, it was blocked. Of course, the degree of depression must be neither too small nor too great. According to their interpretation, the blocked impulse failed to pass because it failed to cause a response of the more strongly depressed region. Thus a proper orientation of less and more depressed areas in a bundle-branch block would make possible the appearance of Type I partial block by protecting the region of greater depression from the effect of the impulse from the other ventricle. It is this latter effect which, as Wilson and Herrmann[21] believe, ordinarily prevents the appearance of partial bundle-branch block.

In this connection it is interesting that in accounting for a human case of irreciprocal conduction in which, in the presence of complete A-V block, there was V-A conduction, Wolferth[22] was independently forced to assume that the same orientation of more and less depressed muscle was present which Ashman and Hafkesbring found by experiment did produce the condition. Other anatomical arrangements of the depressed regions in a bundle-branch might make possible the appearance of the 4:3 type of block, as, for example, in Scherf and Shookhoff's[19] experiments, but, with the latter exception, the phenomenon would apparently depend upon unidirectional block. The 2:1 bundle-branch block observed by Leinbach and White and the 4:1, 3:1 block in Slater's case may very possibly have been Type I intraventricular block and be explained on this basis.

## COMMENTS RELATIVE TO ADAPTABILITY OF THEORETICAL CONSIDERATION TO CLINICAL CASES

As an important consequence of our analyses, there emerges the fact that it is impossible to recognize the type of intraventricular block excepting in rare cases. In all supposed instances one must be sure that the heart rhythm is regular. One example is hypothetical since it has not been observed in man. That is the occurrence of a narrow QRS, its gradual prolongation for one or more additional cycles, and its abrupt return to the narrow form. As a variant of this, one might find a narrow cycle, next a much wider one, and then one or more still wider, but equal QRS complexes of typical bundle-branch block configuration. This sequence of events should repeat in each of these instances, of course. These would represent bundle-branch block of Type I. Another example, here Type II, would be the occurrence of two or more narrow, followed by two or more wide complexes.

The cases herein reported, in which there is an abrupt transition from wide to narrow form, or vice versa (see especially Figs. 1 and 3), clearly represent intraventricular block of Type II and are, so far as we know, the only cases on record which can be proved to belong to that type. Perhaps the critic will be inclined to dispute this point. He will discover that there is usually a very slight slowing of ventricular rate when the improvement in conduction occurs, and will attribute the improvement to that factor. In this he will, no doubt be right. But at the same time, the evidence for block of Type II is unshaken, as is demonstrated by the narrowness of the QRS complexes of normal configuration, as compared with those during the block in Case 1. The latter average at least 0.16 second in duration (confirmed by the three leads) compared with 0.08 for the former. In block of Type I, the slight slowing might occasion a slight change in QRS width, but nothing approaching this degree. This is understandable if we recall that the damaged region will be reached during every cycle by impulses from both sides, and its physiological state will, therefore, remain unchanged. A slight slowing of the heart will not cause a sufficient immediate change in the physiological state to permit such a transition within the time of a single cycle. We are manifestly dealing, therefore, with a Type II block, the only type in which such abrupt changes occur.

The immediate cause of the sudden transition, whether it be alteration in intracardiac blood supply, in pressure, or in some other factor, is not to be regarded as essentially different from the causes of a relatively gradual transition. Under the circumstances of a rather sharply localized region of depression in a bundle-branch, yet one capable of producing block, but causing little or no slowing of the intraventricular impulse, the only possible result of a gradual improvement in the functional condition is an abrupt transition from block to practically undelayed conduction.

In conclusion, we suggest that in those cases of gradual transition from apparently complete bundle-branch block to normal intraventricular conduction, the functional change in the bundle-branch has affected a stretch of tissue of some length. Such a block is, therefore, generally to be regarded as an intraventricular counterpart of A-V block of Type I. Where no transitional complexes occur, but the change is sudden, the defect is the intraventricular counterpart of A-V block of Type II with normal P-R intervals, and the affected stretch of muscle is presumably short.

## THEORETICAL CONSIDERATIONS REGARDING THE DANGER OF VENTRICULAR FIBRILLATION IN BUNDLE-BRANCH BLOCK

One of the points stressed in this paper is the increased operative risk during bundle-branch block in those patients in whom the condi-

tion is a transient one. The outstanding danger appears to be ventricular fibrillation.

From the theoretical side it is not difficult to see why the danger is present. The sequential invasion of the two ventricles, the one by the supraventricular impulse, the other by the impulse from the opposite ventricle, means that the former begins its recovery earlier. At the same time the ventricle whose bundle branch is damaged is in part depressed; regions of muscle are presumably present through which conduction is slow. Now if, to the already existing depression, there is added the effect of the anesthetic, conduction of the impulse in some pathway may become slowed still more. Thus, by the time impulse has travelled through this region, the muscle beyond, which was activated relatively early, may have passed out of the absolutely refractory state, and re-entry is possible. With re-entry the impulse can again swing through the same circuit. Ventricular tachycardia (or flutter) progressing rapidly to fibrillation is the consequence. If, to these factors, irreciprocal conduction or unidirectional block be added, the possibility of fibrillation is much easier to understand. Garrey[23] and Mines[24] agreed on the importance of one-way block for the establishment of fibrillation, and this view has recently been supported by Schmitt and Erlanger.[25]

## SUMMARY

1. Eight cases of partial bundle-branch block of varying degrees are presented with abstracts of their clinical histories, complete physical and laboratory data and electrocardiographic studies.

2. Three unusual cases of transient Type II, intraventricular or bundle-branch block are recorded with sudden transition from complete bundle-branch block to normal intraventricular conduction times in response to respiratory maneuvers. The possible mechanical or nervous factors concerned in the production of the changes are considered to be anoxemia as well as fatigue. Vagus effect may be contributory.

3. We have stressed especially the importance of the recognition of this transient type of disturbance because of its better prognostic outlook. When present it must be relieved by therapeutic rest before necessary surgical or intravenous procedures are to be undertaken.

4. The increased risk assumed in submitting patients, in the presence of bundle-branch block, to a procedure that may apparently only slightly affect the blood pressure and the heart is emphasized.

5. The theories of partial heart-block with special reference to and the intraventricular counterparts of the accepted Types I and II of auriculoventricular types are discussed at some length.

6. The theoretical reasons for the danger of precipitating fatal ventricular fibrillation in the presence of bundle-branch block are given.

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# OBSERVATIONS ON THE ETIOLOGY AND TREATMENT OF PAROXYSMAL VENTRICULAR TACHYCARDIA*

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ALTHOUGH the subject of ventricular tachycardia has been exceedingly well studied, the total number of cases reported in the literature has been small. In this communication three additional cases are reported, two of the usual type and one of the alternating bidirectional variety. In one case the paroxysms were associated with persistent atrioventricular rhythm, a combination not previously reported in the literature. In addition, the effectiveness of quinidine therapy in the alternating bidirectional variety of ventricular tachycardia is demonstrated for the first time.

## CASE REPORTS

CASE 1.—*Diagnosis: Hypertensive heart disease, congestive heart failure, ventricular tachycardia, digitalis intoxication.* L. B., a negro laborer, 47 years old, entered the John Sealy Hospital January, 1924, because of an acute bronchitis. The routine examination revealed a blood pressure of 160/100 mm. Hg. No cardiac enlargement was demonstrable either by physical examination or by roentgenological study. The urine showed a trace of albumin. He was not seen again until September, 1927, when he re-entered the hospital complaining of shortness of breath and swelling of the feet of about two months' duration. Examination at this time revealed moderate cardiac enlargement, a blowing mitral systolic murmur, enlargement of the liver, moist râles in the base of both lungs, and edema of the lower extremities. The systolic blood pressure ranged from 165 to 180, and the diastolic from 105 to 115. The blood Wassermann was negative. The urine showed a persistently low specific gravity. The blood chemistry was normal. The electrocardiogram showed a moderate degree of left ventricular preponderance, slurring of QRS complexes in all leads, occasional auricular and ventricular premature beats, and inversion of the T-wave in Leads I and II. Following digitalization he made a rapid and satisfactory recovery. Shortly after his discharge he discontinued treatment and began doing hard manual labor on the docks. He re-entered the hospital in October, 1927, in essentially the same condition as on the preceding admission. After a prolonged period of bed rest and the usual therapeutic procedures he improved and was discharged practically free of symptoms. He was seen at irregular intervals in the Out-Patient Department until January, 1928, when he was again hospitalized because of congestive heart failure. On this admission gallop rhythm and alternation of the pulse were noted for the first time. The electrocardiogram showed no significant changes over those taken on previous admissions. The response to treatment was much slower than previously, and after prolonged treatment he was sent home to spend the remainder of his life as a cardiac invalid.

On May 16, 1929, he was brought to the emergency room of the hospital. He appeared to be in great distress. The mental state was that of a stupor, and he

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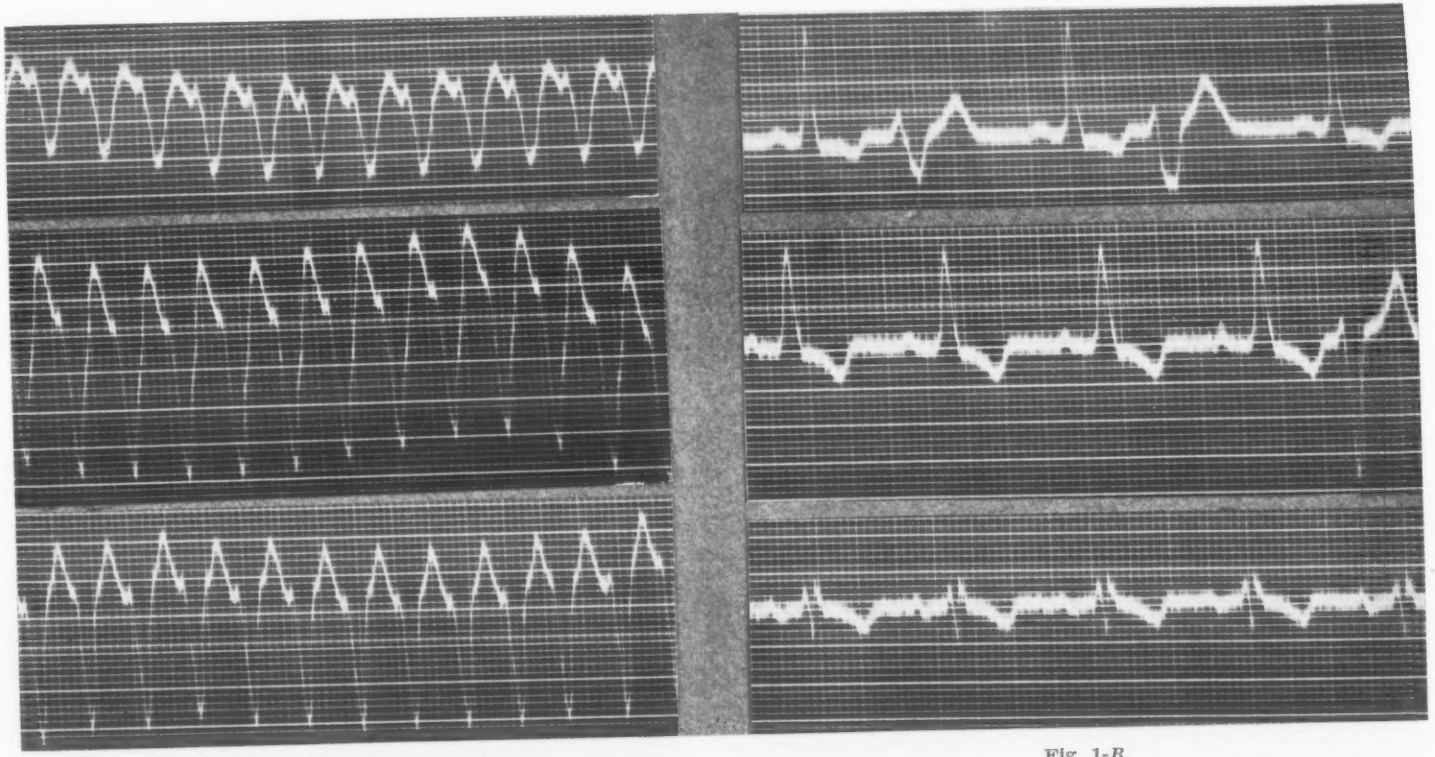

Fig. 1-*A*.

Fig. 1-*A*.—Case 1. Three usual leads. Ventricular tachycardia, rate 220. The P-waves are not discernible. (In this and the subsequent electrocardiograms distances between abscissae represent 10-4 volts, and time is in fifths of a second.)

Fig. 1-*B*.

Fig. 1-*B*.—Case 1. Three usual leads. Curve taken after period of tachycardia showing normal mechanism with frequent ectopic ventricular beats. The shape of the premature ventricular complexes is similar to those occurring during the paroxysm.

could be aroused only with difficulty. The pulse was imperceptible at the wrist. The blood pressure was too low to be taken. On auscultation of the heart the rate was found to be above 200, apparently quite regular, but there seemed to be some variation in the intensity of the individual heart sounds. Moist râles were heard throughout the chest. Six mg. of strophanthin were given intravenously without any apparent effect. The electrocardiogram showed a ventricular tachycardia with a rate of 220 (Fig. 1 *A*). At 10:30 o'clock, 0.3 gm. of quinidine sulphate was given by mouth, followed by 0.6 gm. at 11 o'clock. There was a sudden return to normal rhythm at 11:20 o'clock. The rate was 75, regular except for an occasional premature beat, and the blood pressure was 105/80 mm. (Fig. 1*B*). After recovery he stated that he had been having similar attacks for about one month. He had been taking digitalis at irregular intervals for the past six weeks. The attacks came on suddenly without apparent cause, lasted from a few minutes to several hours and ceased quite abruptly. During the attacks he said that he

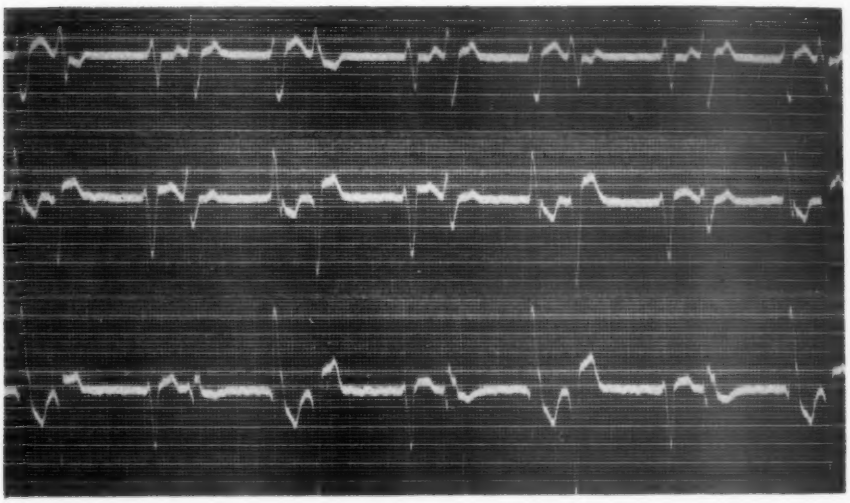

**Fig. 2.—Case 1. Leads I, II, and III. Curve taken following digitalis intoxication. Auricular fibrillation is present with complete heart-block and idioventricular rhythm. The ectopic beats appear in couples and in the majority of cases show alternation in direction.**

became quite short of breath, very weak, and had a feeling of constriction in his chest. The paroxysm which brought him to the hospital had lasted eighteen hours.

For two or three days following the attack the pulse was quite irregular, due to many premature beats which occasionally produced a bigeminy. There was no edema present. He was placed on 0.6 gm. of quinidine sulphate daily. After a few days the pulse became quite regular. On May 29, 1929, while taking a bath, he had another paroxysm which lasted about an hour. The curves taken at that time were identical with the former ones. He was given 0.6 gm. of quinidine sulphate by mouth, and the paroxysm ceased twenty minutes later. On June 6, 1929, he suffered another attack which lasted about fifteen minutes. The quinidine was increased to 1.3 gm. daily. His general condition had improved a great deal, and he was discharged from the hospital and advised to continue taking 1.3 gm. of quinidine daily. On June 25, 1930, he appeared in the clinic and stated that he had suffered no more attacks but that he had become very short of breath. He had been taking the quinidine as prescribed. Examination showed the patient to be very

dyspneic, the liver was greatly enlarged, and there was a pitting edema extending well above the knees. The pulse was regular, rate 96, and alternation was present. The blood pressure was 168/105 mm. Hg. He was given a prescription for thirty 0.1 gm. tablets of the powdered leaf of digitalis and advised to take two tablets four times daily until fourteen had been taken and then to return for observation. After returning home his condition became much worse, and instead of returning to the hospital he continued taking the digitalis until he had exhausted his supply, i.e., 3 gm. of the powdered leaf of digitalis in less than four days. He was brought to the emergency room June 30, 1930, in a paroxysm which had lasted four hours. It ceased a few minutes after taking an electrocardiogram which was identical with those taken previously during the paroxysms. He stated that he had been having five to six attacks daily since the second day after he began taking digitalis. An electrocardiogram taken after the paroxysm revealed the following: auricular fibrillation, complete heart-block, and idioventricular rhythm (Fig. 2). Quinidine sulphate was administered in doses of 0.6 gm. every four hours. He had one paroxysm during the night which lasted only a few minutes. Dyspnea was marked, and a generalized anasarca was present. He died suddenly the following morning.

*Autopsy Findings.*—The heart weighed 950 gm. There were a few adhesions between the left ventricle posteriorly and the parietal pericardium. There was marked dilatation of the right side of the heart. The left ventricular wall was three centimeters in thickness. The valves showed no significant changes. In the tip of the left ventricle near the endocardial surface a healed infaret one centimeter in diameter was found. The first part of the aorta showed some dilatation and a few atheromatous plaques. The coronary arteries were moderately thickened and tortuous. Microscopically, the kidneys showed evidence of a chronic diffuse nephritis.

The curves taken during the paroxysms of tachycardia in this case do not fulfill all the criteria cited by Robinson and Herrmann,[1] as the P-waves are not distinguishable. However, the form of the ectopic beats seen in the curve taken after cessation of the paroxysm are similar to those ventricular complexes seen during the rapid rate. In addition, the clinical course of the tachycardia and the effectiveness of quinidine therapy establish the diagnosis, and readily differentiate it from the condition with which it most likely would be confused, namely, auricular flutter with a one to one response. The curve (Fig. 2) taken following the severe digitalis intoxication is quite unusual. Auricular fibrillation is undoubtedly present with, perhaps, complete auriculo-ventricular block, as none of the ventricular complexes conform to the supraventricular type. Four different types of ventricular complexes are seen, each recurring at perfectly regular intervals. The complexes appear in couples and show alternation in direction in the majority of instances. The rôle of digitalis as a precipitating factor of the paroxysms of ventricular tachycardia in this case cannot be questioned. The condition had been perfectly controlled by quinidine for several weeks, the paroxysms reappearing shortly after the institution of digitalization, and increasing greatly in frequency as the administration of the drug was continued.

CASE 2.—*Diagnosis: Hypertensive heart disease, congestive heart failure, coronary occlusion, chronic uremia, ventricular tachycardia.* E. B., a white man, fifty-four years old, an engineer by occupation, entered the hospital June 22, 1930, complaining of shortness of breath and swelling of the feet. These symptoms first appeared about seven months ago and had been progressively becoming worse. He had been told by several physicians that his blood pressure was over 200. Four nights before coming to the hospital he had a severe attack of dyspnea associated with intense precordial pain. The pain was most intense over the lower end of the sternum and under the left scapula. This pain persisted for about four hours. Since this attack his condition had become much worse, and of late he had been having severe

headaches and attacks of intractable vomiting. The past history was irrelevant. The family history was interesting in that his father, mother, and one sister had died of kidney trouble.

On physical examination the patient was quite dyspneic. The heart was greatly enlarged. A moderately loud blowing systolic murmur was heard at the apex. The pulse was quite irregular due to many premature beats, which occasionally produced long runs of bigeminy. The blood pressure was 140/80 mm. Hg. The peripheral

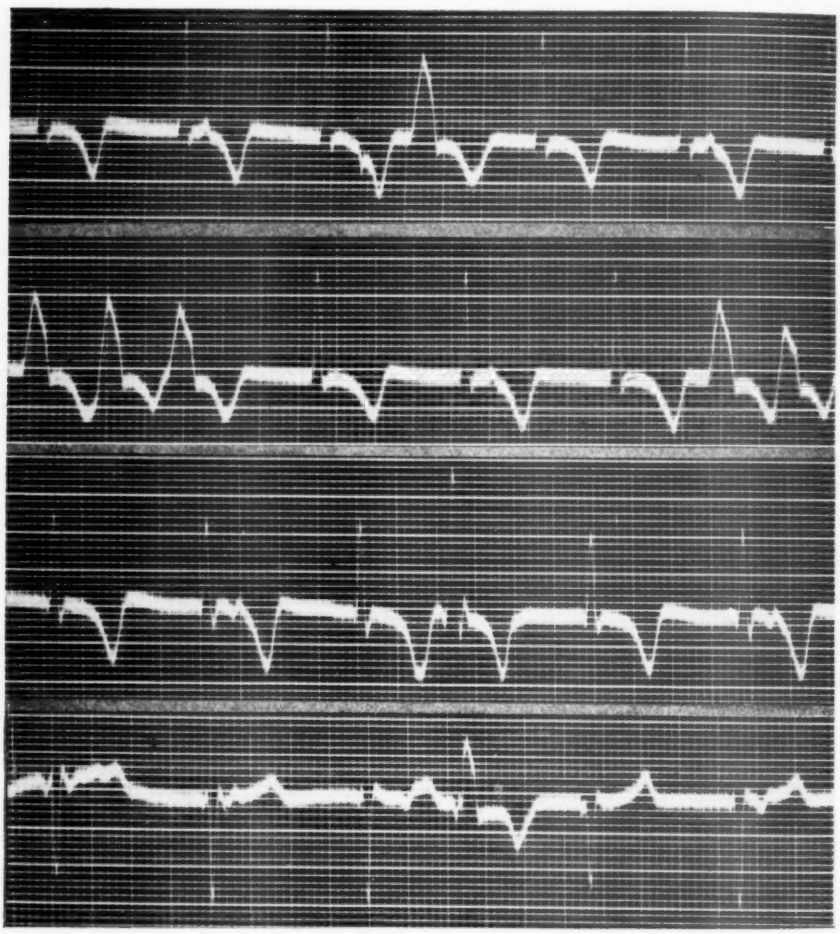

Fig. 3.—Case 2. Three usual leads, upper two strips are Lead I. The offset and onset of a paroxysm of ventricular tachycardia are shown in the second strip. The rate (taken from another portion of the record) is 160. Atrioventricular rhythm is present. There is some evidence of retrograde heart-block. Note the marked inversion of the T-waves in the first two leads.

vessels were markedly sclerosed and showed some beading. The liver was greatly enlarged, and there was some ascites present. Moist râles were heard over the chest posteriorly. There was a pitting edema of the lower extremities. The routine blood count revealed a marked secondary anemia. The blood urea was 100 mg., and the creatinine was 7.5 mg. per 100 c.c. of blood.

The patient had been under the treatment of a physician in the city for several months and was taking digitalis up to the time of admission to the hospital, how-

ever, it was impossible to ascertain the amount that he had taken. The day following admission it was noticed that in addition to the many premature beats, there were short paroxysms of tachycardia lasting from a few seconds to as long as thirty minutes. The rate during the paroxysms was approximately 150, and the rhythm showed a slight irregularity. The onset and offset were abrupt. Vagal stimulation had no effect on the rate. An electrocardiogram showed atrio-ventricular rhythm with runs of ventricular tachycardia during which the rate was 160 (Fig. 3). He was immediately placed upon 0.75 gm. of quinidine sulphate daily. The premature beats decreased greatly in number, and no more paroxysms of tachycardia were noted. Subsequent curves taken revealed only occasional ventricular premature beats; however, the atrio-ventricular rhythm persisted. In spite of treatment his general condition became rapidly worse, and he died a week later in uremic coma, the terminal event being a hypostatic pneumonia. Autopsy was refused.

The rôle of digitalis in the production of the arrhythmia in this case is not quite so evident as in the other cases, although it was apparently a factor. The patient had been taking digitalis for some time, but it was impossible to ascertain the exact amount taken. Atrio-ventricular rhythm is known to occur occasionally as a result of digitalis administration, but it is not generally thought of as being a toxic manifestation of the drug. The runs of bigeminy noted on admission offer further evidence that he had probably received too much of the drug. The history of the sudden onset of severe precordial pain, the prostration, the fall in blood pressure, and the progressive heart failure furnish sufficient clinical grounds for the diagnosis of coronary occlusion. The marked inversion and the character of the T-waves would tend to confirm this diagnosis.

CASE 3.—*Diagnosis: Syphilitic heart disease (?), aortic regurgitation, congestive heart failure, auricular fibrillation, ventricular tachycardia.* K. C., a white man, sixty-five years old, a watchman by occupation, was sent into the John Sealy Hospital March 28, 1929, complaining of intense cramping pain in the lower part of the abdomen. Examination revealed a strangulated left inguinal hernia. A careful cardiac examination was not done at that time. He was immediately subjected to a surgical operation, the strangulation relieved and the hernia repaired. Local anesthesia (novocaine) was employed. Post-operative recovery was uneventful, and he was discharged three weeks later in good condition.

He returned to the hospital June 27, 1929, complaining of shortness of breath and swelling of the feet which began two weeks previously, and which had become progressively worse. The family history was irrelevant. Twenty years previously he had had a bad attack of gonorrhea which was followed by a stricture of the urethra. He denied ever having had a penile sore. On physical examination there was some obesity. Dyspnea was marked. The chest was quite emphysematous. The heart was greatly enlarged downward and to the left. On auscultation there was heard at the aortic area a soft to-and-fro murmur. The heart rate was rapid and quite irregular, due to many premature beats. The blood pressure was 150/65 mm. Hg. A moderate amount of arteriosclerosis of the diffuse type was present. Moist râles were heard over the entire chest, the liver was enlarged and tender, and a pitting edema extended well up the thighs. The electrocardiogram showed sinus rhythm, slurring of the QRS complexes in all leads, inversion of the T-wave in Leads I and II, and ventricular premature beats. Following digitalization and rest in bed the symptoms and the edema disappeared. He was discharged July 7, 1929, and advised to continue taking a maintenance dose of digitalis.

He returned to the Out-Patient Department at regular intervals for observation. He remained fairly well until February 17, 1930, when it was necessary to hospitalize him again because of congestive heart failure. On this admission the physical examination was essentially the same except that the degree of failure was more

marked. The blood pressure was 150/80 mm. Hg. Alternation of the pulse was noted. As before, the pulse was quite irregular due to many premature beats. An electrocardiogram was similar to that taken on the previous admission (Fig. 4). The blood urea nitrogen was within normal limits. The blood Wassermann was frankly negative. It was necessary to resort to the use of the mercurial diuretics to mobilize the edema. After three weeks of energetic treatment he was discharged edema-free, but the dyspnea, though lessened, still remained.

He returned to the hospital two weeks later again showing marked dyspnea and edema. Examination May 5, 1930, revealed a generalized anasarca. The pulse was still irregular because of many premature beats, and the blood pressure was 140/68 mm. Hg. Intense pulmonary congestion was evident. He had been taking 0.1 gm. of the powdered leaf of digitalis daily since the last dismissal from the hospital. The interne was not cognizant of this fact, and from May 5 to May 18, he received 3 gm. of the powdered leaf of digitalis. The electrocardiogram on admission showed sinus rhythm, whereas a curve taken on May 19, 1930, showed auricular fibrillation

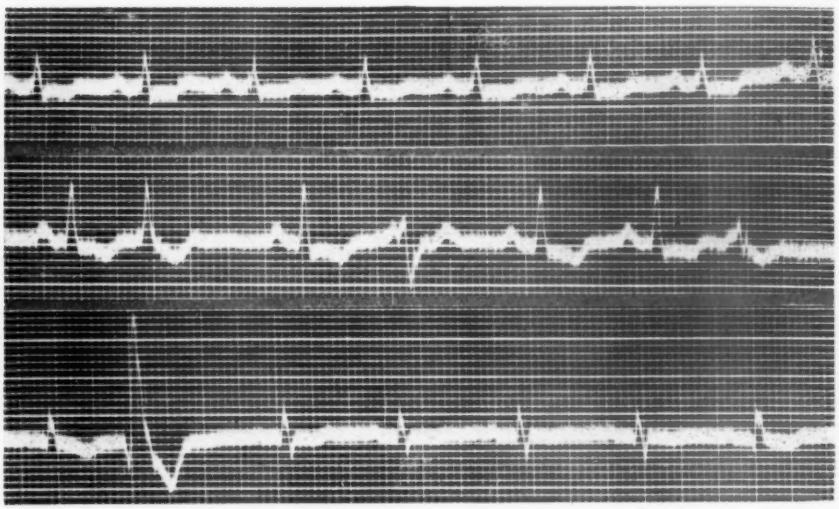

Fig. 4.—Case 3. Three usual leads. Record obtained on February 17, 1930. Sinus rhythm is present with frequent ectopic beats. There is slurring of the ventricular complexes in all leads. The T-waves in Leads I and II are inverted.

with ventricular premature beats producing a bigeminy (Fig. 5*A*). A tracing taken the following day revealed paroxysms of alternating bidirectional ventricular tachycardia (Fig. 5*B*). The next day the frequency and the duration of the paroxysms increased. One paroxysm was observed to last three hours. The digitalis was immediately discontinued and the administration of quinidine sulphate begun, in doses of 0.6 gm. daily. This was increased the following day to 1 gm. daily. Six hours after the quinidine was started the paroxysm ceased and numerous observations failed to reveal any reappearance; however, the auricular fibrillation along with occasional ectopic ventricular beats persisted. The patient showed no response to treatment, the edema being exceedingly obstinate. A few days before death he developed marked mental symptoms. Death occurred May 27, 1930. Autopsy was refused.

On admission this patient was apparently fully digitalized, as he had been taking a maintenance dose of digitalis for several weeks prior to his final entry. When he entered the hospital, sinus rhythm was present along with many ectopic ventricular beats. Due to an oversight he was given digitalis in sufficient amounts again fully

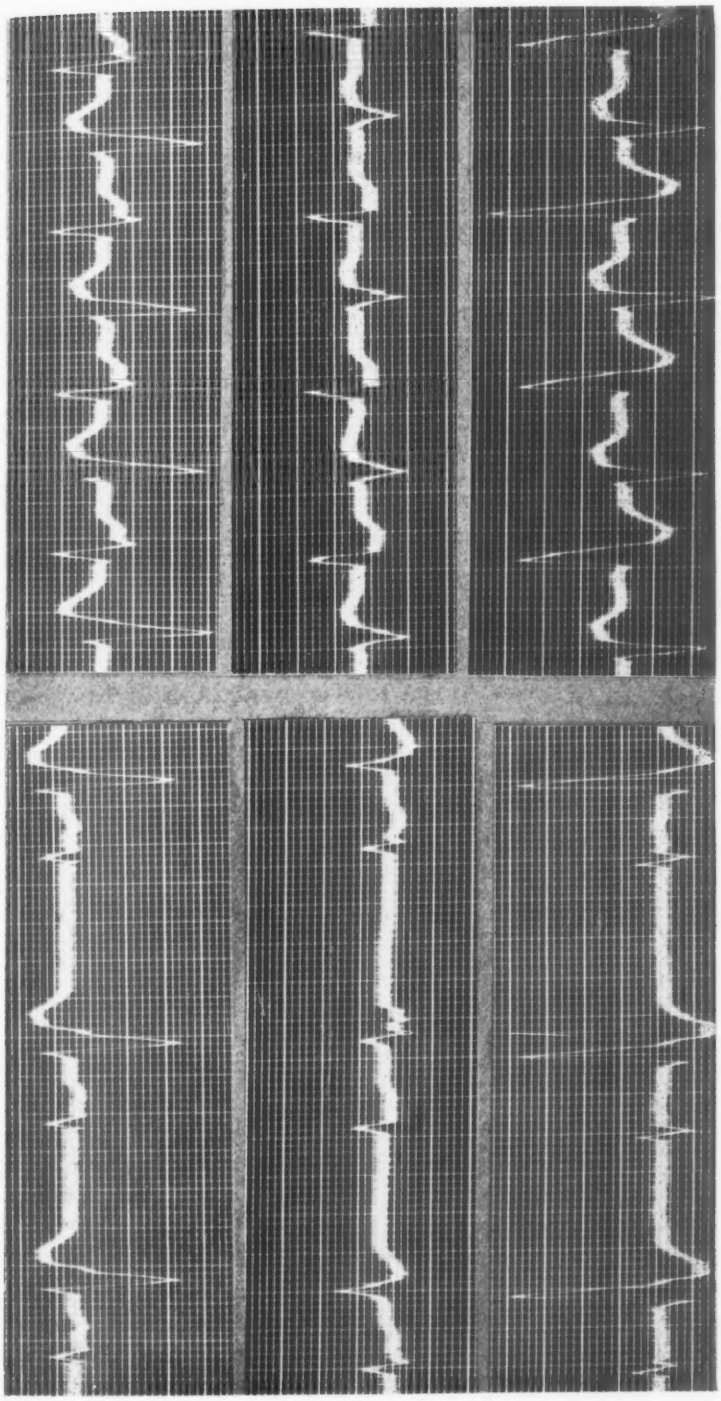

Fig. 5-*A*.

Fig. 5-*A*.—Case 3. Leads I, II and III. Record obtained May 19, 1930, showing auricular fibrillation with ventricular premature beats producing a bigeminy.

Fig. 5-*B*.

Fig. 5-*B*.—Case 3. Three usual leads. Record obtained May 20, 1930. Alternating bidirectional ventricular tachycardia with a rate of 140. In addition to the alternation in direction of the ventricular complexes there is predominantly alternation in the length of cycles.

to bring him under the influence of the drug. Auricular fibrillation appeared after a short time, and was undoubtedly a manifestation of digitalis intoxication. The associated bigeminy would tend to substantiate this contention. Shortly thereafter, the appearance of the paroxysms of ventricular tachycardia were noted. As in the cases reported by Palmer and White[2] there is not only alternation in the direction of the ventricular complexes, but there is also predominantly alternation in the length of the cycles, the interval between an inverted and an upright complex being shorter than that following an upright complex in Leads I and II, whereas the reverse holds true in Lead III. It is interesting to note that the majority of the cases of alternating bidirectional ventricular tachycardia reported were associated with auricular fibrillation.

## DISCUSSION

No definite proof has as yet been advanced as to the underlying mechanism in ventricular tachycardia. For the unidirectional type, most writers advance the theory that the mechanism is similar to that which is generally conceded to produce paroxysmal auricular tachycardia, namely, a single irritable ectopic focus. The two types of tachycardia are similar in that the onset and offset of the abnormal rhythm are abrupt and bear the same relationship to the normal rhythm as do single ectopic beats. The great point of difference, however, is that the action of the heart during paroxysms of auricular tachycardia is notable for its regularity, whereas in the ventricular type, as emphasized by Strong and Levine,[3] a slight but noticeable irregularity occurs. Largely because of this irregularity, and because of the therapeutic response of the condition to quinidine, Levine and Fulton[4] have suggested that the underlying mechanism is a circus movement similar to that seen in the auricle in auricular fibrillation and flutter. The variation in the configuration of the abnormal complexes, which is commonly seen, could be explained on a basis of aberration; nevertheless, it is more logical to assume that it is a result of a variance of the path assumed by the circus, which likewise explains the slight irregularity in rhythm.[2] The unusual curve (Fig. 2) taken in Case 1, following the digitalis intoxication, could possibly be due to a circus movement similar to that producing the paroxysms of tachycardia, its path being greatly altered by changes in the refractory period of the heart muscle, a result of the toxic effect of the digitalis. The possible mechanisms underlying the alternating bidirectional type of ventricular tachycardia have been discussed in detail in the literature.[2, 5] The double ventricular circus movement as suggested by Palmer and White seems most likely, as the condition cannot be adequately explained on the basis of a single circus. Clinically, the two types are identical and can be separated only by electrocardiographic study.

The majority of the cases of ventricular tachycardia have occurred in individuals with advanced heart disease, most of them being in a state of congestive or anginal failure at the time of the onset of the arrhythmia. However, several cases are on record in which no abnor-

mal cardiac findings were demonstrable. The alternating bidirectional variety occurs with greater uniformity in patients with grave forms of heart disease than does the unidirectional type. In all of the cases of the alternating bidirectional form reported, pathological change in the heart was noted; in one instance the only finding was cardiac enlargement, the remainder showed evidence of marked structural cardiac disease. Advanced coronary artery disease and coronary occlusion are important predisposing factors. Coronary occlusion was present in eight out of the ten cases in one series.[4] In approximately one-fourth of the cases reported, cardiac infarction had preceded the onset of the ventricular tachycardia. In patients in whom no organic heart disease is present, the prognosis is essentially good; in those in whom definite organic changes are evident, the prognosis is grave, especially if the alternating bidirectional form of tachycardia is present, the majority of these patients dying in from a few hours to a few weeks.

The relationship of digitalis to the occurrence of ventricular tachycardia has been emphasized by a great many writers on the subject.[6, 7, 8, 9, 10, 11, 12] It undoubtedly plays a very important part, acting largely as the precipitating or exciting factor. Considering all of the cases of both types, the drug had been administered prior to the onset of the arrhythmia in approximately 50 per cent of the cases, and in the majority of these, it was given in excessive amounts. In Case 1 of this group, in which the paroxysms had been completely controlled by quinidine, there was a reappearance shortly after the institution of digitalization, and they increased greatly in frequency and duration as the administration of digitalis was continued. In one of the cases reported by Gilchrist,[12] Case 2, the frequency of the paroxysms was greatly increased by the giving of digitalis. In Cases 2 and 3 of Levine and Fulton's series, the giving of digitalis caused an increase in the rate of the tachycardia, and a similar experience was reported by Orsi and Villa.[13] To the contrary, in the case reported by Hart[14] "small doses of digitalis" caused no recurrence; Wolferth and McMillan,[15] Cases 2 and 3, gave digitalis in full doses after the cessation of the paroxysm without apparent effect as regards recurrence.

The rôle of digitalis as an exciting factor in the causation of ventricular tachycardia is much more apparent after a study of the reported cases of the alternating bidirectional type. Including the case herewith reported there are twenty-two cases recorded in the literature.[2, 5, 6, 7, 8, 9, 12, 13, 16, 17, 18] Of this number, excluding three of Gallavardin's cases[16] in which the records are not clear, all but two cases had received digitalis. Of these seventeen cases, fifteen were said to have received the drug in toxic amounts. In the case of this type reported here, digitalis had been given in sufficient amounts to convert sinus rhythm to auricular fibrillation. In the case reported by Orsi

and Villa,[13] a change from the usual type of ventricular tachycardia to the alternating bidirectional form occurred a few seconds following the intravenous injection of calcium chloride.

Despite the fact that evidence has been adduced to show that quinidine itself may cause ventricular tachycardia,[19, 20, 21, 22] the drug apparently has a specific effect in terminating the paroxysms of tachycardia and preventing their recurrence. In all the cases reported in which the drug has been used, uniform success has been attained. The drug is apparently just as specific in controlling the alternating bidirectional variety as in the usual type, although no definite conclusions can be drawn from its use in a single case. The amount of the drug necessary to produce therapeutic results varies greatly from case to case. On the whole, somewhat larger doses are needed to terminate a paroxysm than is necessary to prevent the recurrence of paroxysms. Very large maintenance doses of the drug have been given over long periods of time without any ill effects. In those cases in which the patient's condition is critical, it is perhaps best to administer the drug intravenously, although its action by mouth is quite prompt.

## SUMMARY AND CONCLUSIONS

1. Three cases of paroxysmal ventricular tachycardia are reported, two of the usual variety and one of the alternating bidirectional type.

2. All three cases were treated with quinidine with uniform success in controlling the arrhythmia.

3. Digitalis, especially when given in excessive amounts, is apparently an exciting factor in the production of ventricular tachycardia. The association is much closer in the alternating bidirectional variety than in the unidirectional form.

4. Because of the close association between coronary occlusion, digitalis, and ventricular tachycardia, digitalis should be administered with extreme caution to patients who give a history of a recent cardiac infarction.

NOTE.—The author is indebted to Dr. R. S. Palmer and other members of the Cardiographic Laboratory of the Massachusetts General Hospital, Boston, and to Dr. George R. Herrmann of New Orleans, for valuable help in the interpretation of the curves from Case 1.

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# THE EFFECT OF VENTRICULAR EXTRASYSTOLES ON THE A-V CONDUCTION TIME OF THE NEXT AURICULAR IMPULSE*†

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IT IS fairly common for the A-V conduction time of the auricular impulse directly following a ventricular extrasystole to be prolonged. A case is here presented in which this phenomenon was quite prominent. This was analyzed in an essentially quantitative manner, because otherwise the nature of the phenomenon could not be thoroughly understood.

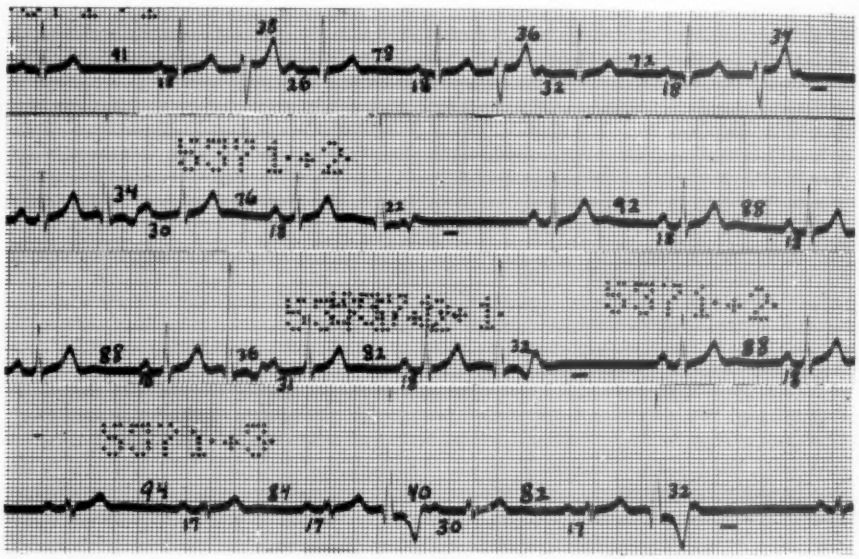

Fig. 1.—Leads I, II, II, and III of Curve 1.

TABLE I (FOR FIG. 1)

| | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | | | | | POST EXTRASYSTOLIC | | | | | | | | |
| R-P | .94 | .92 | .91 | .88 | .88 | .88 | .84 | .82 | .82 | .78 | .76 | .72 | .40 | .38 | .36 | .36 | .34 | .34 | .32 | .32 | .22 | |
| P-R | .17 | .18 | .18 | .18 | .18 | .18 | .17 | .17 | .18 | .18 | .18 | .18 | .30 | .26 | .31 | .32 | .30 | – | – | – | – | |

Fig. 1 shows portions of a curve with frequent right ventricular extrasystoles, after which the next auricular impulse is conducted either more slowly or not at all. This partial—and occasionally com-

*From the Heart Station, Michael Reese Hospital, Chicago, Ill.
†Aided by the Emil and Fannie K. Wedeles Fund for the Study and Investigation of Diseases of the Heart and Circulation.

plete—A-V block is explained as follows: The impulse of the ventricular extrasystole is conducted backward through the common bundle to the A-V node. It is not conducted past the node to the auricle (this would be a retrograde ventricular extrasystole, which has never been proved to occur), but it does renew the refractory period of the node, so that the next auricular impulse finds the node either relatively or absolutely refractory and is accordingly either partially or completely blocked. We place the block in the node rather than in the bundle because the refractory period is normally longer in the node and block is more readily produced there.[1]

The A-V conduction time of every beat depends upon four things: (1) the presence or absence of organic disease of the A-V node or bundle; (2) the alteration of the A-V node or bundle by drugs or other chemical influences; (3) vagus and sympathetic influences *at the time of passage of the impulse through the node;* and (4) the time permit-

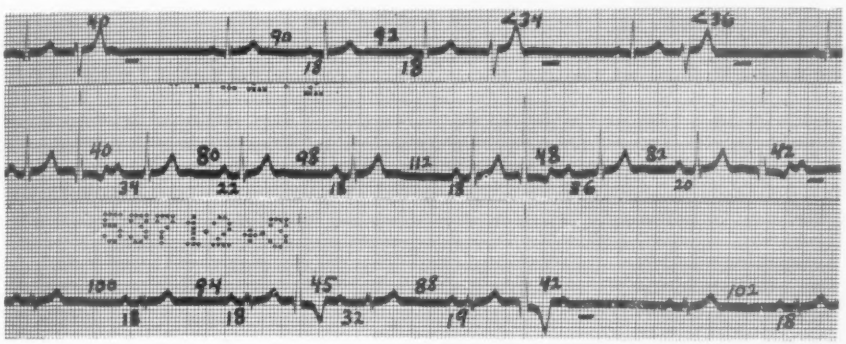

Fig. 2.—Leads I, II, and III of Curve 2, taken two days after Curve 1.

TABLE II (FOR FIG. 2)

| | | | | | | | | | | | | | | | | | POST EXTRASYSTOLIC | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| R-P | 1.12 | 1.02 | 1.00 | .98 | .94 | .92 | .90 | .88 | .82 | .80 | .48 | .45 | .42 | .42 | .40 | .40 | <.36 | <.34 | |
| P-R | .18 | .18 | .18 | .18 | .18 | .18 | .18 | .19 | .20 | .22 | .36 | .32 | – | – | .34 | – | – | – | – |

ted for recovery of the node after the passage of the last preceding impulse. This time interval, which is called the *recovery time,* is measured from the beginning of the preceding QRS complex to the beginning of the P-wave, and is designated by R-P. Other things being equal, the conduction time increases monotonically as the recovery time decreases;[2] but, as is well known, even with a long recovery time conduction may be slowed by nervous influences.

To illustrate these principles I have marked on the electrocardiograms shown in Figs. 1, 2 and 3, the recovery times above the curve and the P-R intervals below. Where the P-wave is partly buried in the T-wave, only an upper limit can be determined for the recovery time; when a beat is completely blocked, the P-R interval is indicated by a

dash. The measurements are tabulated in decreasing values of the recovery time as follows:

It is seen that in general the P-R interval increases as the recovery time decreases; the exceptions most probably indicate temporary changes in tonus of the cardiac efferent nerves. On the whole, A-V conduction is slower in Curve 2 than in Curve 1.

To find out what part of the delayed conduction is due to vagus tone we gave the patient $\frac{1}{50}$ gr. of atropine sulphate hypodermically just after Curve 2 was taken; thirty minutes later Curve 3 was taken. The sinus rate was increased only slightly (from 55 to 59). We see again the same general rule for increase of the P-R interval with decrease of the recovery time:

Whereas before atropine, complete block occurred with a recovery time as long as 0.42 sec., after atropine, there is no instance of complete block until the recovery time is as short as 0.20 sec. Similarly,

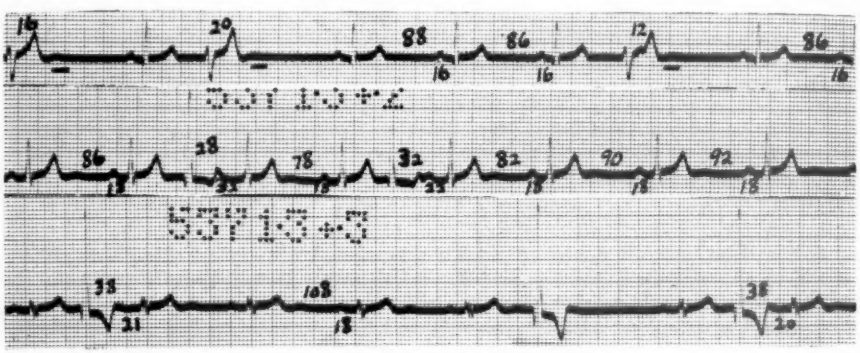

Fig. 3.—Leads I, II, and III of Curve 3, taken on the same day as Curve 2, thirty minutes after atropine.

TABLE III (FOR FIG. 3)

| | | | | | | | | | | POST EXTRASYSTOLIC | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| R-P | 1.08 | .92 | .90 | .88 | .86 | .86 | .86 | .82 | .78 | .38 | .38 | .32 | .28 | .20 | .16 | .12 |
| P-R | .18 | .18 | .18 | .16 | .16 | .16 | .18 | .18 | .18 | .20 | .21 | .22 | .32 | – | – | – |

before atropine we have a P-R of 0.36 sec. with a recovery time as long as 0.48 sec. and after atropine a P-R of only 0.20 sec. with a recovery time as short as 0.38 sec. Thus A-V conduction is greatly improved after atropine. After atropine there is no delay in conduction beyond normal limits (0.22) until the recovery time is reduced to 0.28 sec. or less than half the recovery time (0.65 sec.) at normal sinus rhythm (rate 72, PR = 0.18), and there is no complete block until the recovery time is reduced to 0.20 sec. or less than one-third the normal. This marked improvement in conduction indicates that the A-V block before atropine was due to vagus influence and not to organic disease. To rule out a possible sympathetic depression adrenalin was injected

on a subsequent day; this had no effect on the block, so that it appears to have been the vagus which was the controlling factor, though the patient had had no digitalis or other vagus stimulant.

These observations indicate that the effect of a ventricular extrasystole on the A-V conduction of the next auricular impulse is no different in nature from the effect of an auricular extrasystole with the same recovery time on its own A-V conduction. It follows that *complete block of the auricular impulse directly following a late ventricular extrasystole has the same significance as a blocked early auricular extrasystole.*

I wish to express my thanks to Dr. Louis N. Katz for his helpful discussion and his valuable criticism.

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# Department of Clinical Reports

## A CASE OF MALIGNANT ENDOCARDITIS (PNEUMOCOCCAL), WITH EARLY CALCIFICATION AND WITH CALCAREOUS RENAL EMBOLI

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THIS case is recorded for two reasons.

First, it shows the great rapidity with which calcification can take place in newly-formed vegetations on an infected heart valve.

The second point of interest is the presence in the arterioles of the kidney of calcified emboli. These have caused, not infarction by occlusion, but hemorrhage by trauma in the neighboring renal substance.

Whereas it is always assumed that emboli in cases of malignant endocarditis come from vegetations on the heart valves, it is a difficult thing to demonstrate. In this instance, however, there can be little doubt as to the cardiac origin of the calcareous material in the vessels of the kidney.

The patient, a youth of 19 years, was admitted to St. Bartholomew's Hospital, London, on April 23, 1930, with a twenty-four hours' history of malaise, fever, headache, and some mental confusion. He complained chiefly of pain in the back.

On examination, the chest showed impairment of movement, percussion note and air-entry all over the right side, but no added sounds.

The heart was considerably enlarged; mitral and aortic regurgitant murmurs were present, but no presystolic murmur.

The general appearance of the patient and his temperature chart (T:101.4° F., P:96, R:32), together with the chest signs, led to a diagnosis of lobar pneumonia.

There was a vague history of rheumatic disease in childhood which might have accounted for the heart signs.

During the following three days the lung signs on the right side cleared up, but the patient did not feel any better, although the chart on the evening of the fourth day suggested a crisis. On the fifth day he had his first rigor. Rigors followed at the rate of 2 or 3 daily. A few days later the patient complained of transient joint pains and occasional numbness of the extremities. The heart sounds were found to alter slightly from day to day. Blood culture was made on the ninth day and grew pneumococci (Type III). Sudden mistiness of vision in the right eye occurred and retinoscopy showed a pale quadrant in the fundus. Petechiae began to appear and became very numerous on the neck and chest: in a few days the body was covered with them. Red blood cells in abundance now began to appear in the urinary deposit. The patient's mental condition became rapidly worse: drowsiness, low delirium and an almost "Parkinsonian" facies. There was increasing pallor.

A course of mercurochrome injections was begun without benefit, and death occurred on May 13, on the twenty-third day of the illness.

The spleen was not palpable at any stage of the disease and there were no painful nodes in the fingers.

At autopsy, the body was that of a well-covered youth.

There were numerous petechiae over the skin, especially about the shoulders.

Internally, minute hemorrhages were seen on the meninges, the trachea, the pleurae, the pericardium, the peritoneum, and the capsules of the kidneys.

The lungs, both macroscopically and microscopically, showed congestion.

The heart: The pericardium contained about 100 c.c. clear fluid. There were dilatation and hypertrophy of all the chambers. The mitral valve showed past and recent disease. The bases of the valve were thick and fibrosed from old damage, but superimposed on these were recent friable vegetations, which had almost destroyed the cusps. These vegetations were large and cauliflower-like, one being about 2 cm. in diameter (see Fig. 1). They spread from the mitral valve to the wall of

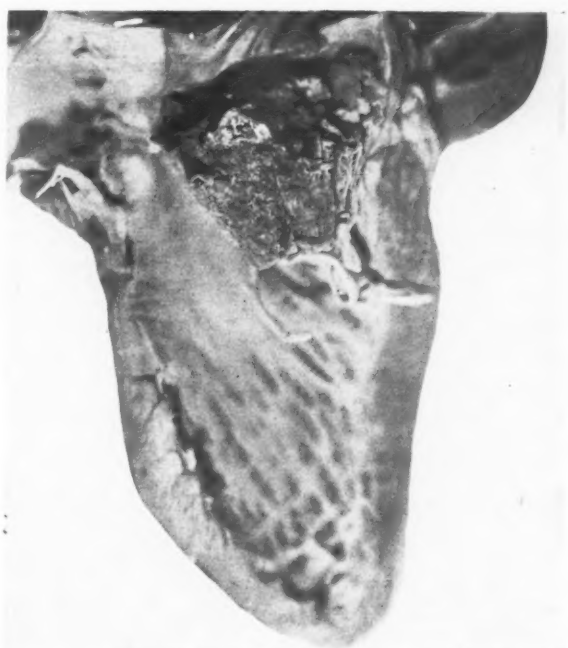

Fig. 1.—A recent vegetation on the mitral valve showing areas of calcification (photograph by A. V. Cobbett).

the auricle, down the chordae tendineae, many of which were eroded, and along the wall of the ventricle to the aortic valve. The latter showed minute recent vegetations and fenestration, but no old scarring.

The most striking feature of the mitral vegetations was the presence of small calcified areas on their surfaces. The rapidity with which these calcified areas must have formed may be judged from the history of the case.

The liver was large and "greasy" and showed microscopically congestion and fatty degeneration.

The spleen was large and soft, and a large number of recent pale infarcts were seen raised above the surface.

The kidneys also contained pale infarcts, but there were in addition many small areas of hemorrhage. Histological examination of these areas showed that the small vessels, and even the glomeruli, in the neighborhood of these hemorrhages contained

particles of calcified material. These particles lay actually within, but not actually blocking, the lumina of the vessels and presumably came from the fragile, partially calcified vegetations on the mitral valve (see Figs. 2 and 3).

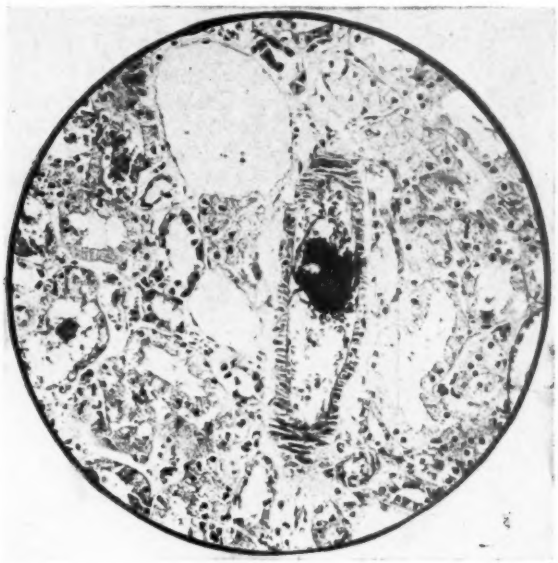

Fig. 2.—Calcified embolus in a small renal vessel (photomicrograph by A. V. Cobbett).

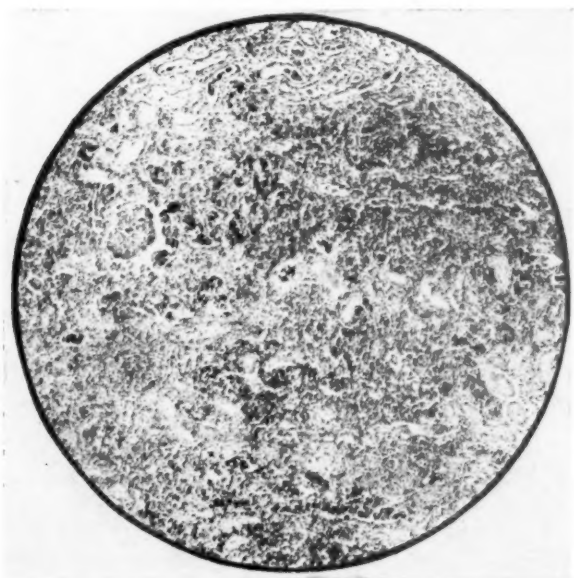

Fig. 3.—Hemorrhage in neighboring kidney substance (photomicrograph by A. V. Cobbett).

It seems probable that the hemorrhages have been caused by the sharp calcareous emboli tearing and damaging the near-by arterioles and capillaries of the kidney.

We thank Professor Fraser for permission to publish this case.

# ANGINA PECTORIS IN A YOUNG ADULT*

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THE recorded incidence of Heberden's angina pectoris in children and young adults is so low that it would seem desirable to have reports of additional cases. White and Mudd,[1] who reviewed the subject in 1927, were able to collect from the literature only forty-two authenticated cases of angina pectoris in persons less than thirty years of age; to these they added eight cases of their own. Stolkind's paper,[2] which appeared almost simultaneously, listed twenty-nine cases, including four which he himself had observed and several which had apparently escaped the attention of White and Mudd. Since that time there have been only two additional reports (Dotti,[3] Levin[4]). It is likely, therefore, that the comprehensive total of cases does not exceed sixty-five or seventy. The cases of paroxysmal cardiac pain reported by Schwartz,[5] as he himself points out, present certain features which are irreconcilable with Heberden's angina pectoris as it is generally conceived.

## REPORT OF CASE

*History.*—The patient, a woman, was born in 1902, and except for a great deal of tonsillitis, which was not diminished in frequency or severity by a "tonsil clipping" operation in 1909, was an unusually healthy child. In 1917 she was seized with severe tonsillitis, followed immediately by acute rheumatic fever, characterized by migratory synovitis and pain over the heart. Within three weeks her physician detected endocardial involvement and cardiac arrhythmia. The high fever began to decline after six weeks; and two months after the onset, although the patient had a rapid heart rate and slight air hunger, she was allowed to sit up in bed. A few weeks later she began to experience chilly sensations, and became once more acutely ill with high fever, rapid pulse and respiration, dull pain in the left chest and dry cough. She grew worse steadily, and after ten days had some sort of "sinking spell" lasting five minutes and characterized by extreme air hunger and apparent loss of consciousness. The fever continued for ten days more, falling by lysis. Coughing was continuous and very painful, and finally became productive of a moderate amount of sputum, at first blood-streaked, later purulent. Although a diagnosis of pneumonia of the left lower lobe, with "heart complications," was made, it is more than likely that acute pericarditis with effusion, and acute endocarditis, possibly with pulmonary emboli, were the actual pathological processes underlying this illness. Convalescence was very slow, lasting more than a year, but at last the patient regained much of her former vigor and returned to school. She completed her last three years of high school without further disability. During this time she was very active, but noticed nothing more than considerable shortness of breath after exertion until the last few months of her senior year, when she began to tire easily and to faint frequently.

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In January, 1923, the patient entered a nurses' training school. Two months later she was ill for a week with tonsillitis, high fever, cough and generalized aching. In May she went to bed with heart failure, and it was at this time that her aortic valve lesion was discovered. By the middle of July she was back on duty, had her tonsils removed, and continued without further interruption until December, when she was subjected to a severe emotional shock (attempted rape). The patient is very idealistic and of extremely sensitive temperament, and this experience precipitated her first attack of angina pectoris (at the age of twenty-one years). She said that she felt as if her chest were being crushed. The attacks of angina kept recurring, and in May, 1924, she was forced by increasing cardiac disability and angina to discontinue her training.

From June, 1924, until April, 1928, she worked intermittently as a "practical" nurse, during which period her activities were interrupted at least as often as twice a year by attacks of heart failure which necessitated many weeks in bed. In 1924 and 1925 she was free from angina pectoris for as long as six months at a time, but in 1926, 1927 and 1928 the seizures increased in frequency, as well as severity, until the intervals became as short as from one to three weeks. Badly discouraged, she twice attempted suicide, the second time by swallowing mercuric chloride in August, 1927. Following this she had albumin and casts in the urine for a time, and ever afterward an abnormally high blood pressure.

About the first of January, 1928, the patient had an upper respiratory tract infection which was followed by six months of cardiac invalidism and fever. During this illness she suffered considerably from a choking sensation, dysphagia and difficult breathing, and an abnormal pulsation made its appearance in the suprasternal notch. These manifestations led her physician to make a diagnosis of acute rheumatic aortitis. By June the patient was able to get about once more, and in August, 1928, she was admitted to the University Hospital.

*Physical Examination.*—The patient was an obese young woman of healthy appearance, weight was 215 lb., height 5 feet, 5 inches. There were no signs of syphilis, and aside from the cardiovascular system no objective observations worthy of record.

All of the essential physical signs of aortic regurgitation were readily demonstrable, *viz.*, pronounced hypertrophy of the left ventricle, a celer pulse of abnormally large volume, and a diastolic murmur originating at the aortic orifice. There was nothing to indicate the presence of any other valve lesion.

Enlargement of the ascending portion of the aorta was betrayed by the ready accessibility of the innominate artery in the suprasternal notch, a vigorous systolic impulse and pronounced diastolic impact over the aortic area, parasternal dulness in the second intercostal space to the right of the sternum, and an accentuated aortic second sound. The last named sign of an abnormally accessible aorta was particularly noteworthy in this case because of the partial replacement of the sound by a loud diastolic murmur.

In spite of the central leak, the minimum diastolic arterial pressure tended toward a normal, or slightly increased, level. An average of fifteen measurements made under widely varying conditions was 81 mm. Hg. Only twice was it found to be below 70 even when measured immediately after the administration of amyl nitrite. The highest figure recorded was 100, the lowest, 60. Similarly, the average maximum systolic pressure of 185 mm. Hg. was more than commensurate with the intrinsic demands of the patient's aortic regurgitation. These facts were taken to indicate an increase of arteriolar resistance, a factor which may well have contributed to the angina pectoris.

There was little evidence of stasis proximal to either ventricle. Most of the 35 per cent reduction of vital capacity could be explained by obesity, and the lungs were free of moisture. Slight edema of the ankles occurred from time to time, but engorgement of the liver or veins of the neck was never demonstrable.

*Laboratory Examination.*—An electrocardiogram showed normal cardiac mechanism, preponderance of the levocardiogram, and, in Lead III, an iso-electric P-wave, a slightly inverted T-wave, and slurring of QRS. The blood Wassermann reaction was negative. Renal resourcefulness, as measured by the usual methods, was undiminished. The urine and blood were normal. Teleroentgenograms succeeded in giving an indication of the left ventricular hypertrophy, and were reported also as showing "accentuation of the aortic knuckle."

*Summary.*—History of repeated tonsillar infections, rheumatic fever, pancarditis, aortitis, myocardial failure, angina pectoris, poisoning by mercuric chloride. Presence of left ventricular hypertrophy, celer pulse of large volume, aortic diastolic murmur, signs of an abnormally accessible ascending aorta, elevation of arterial blood pressure. No signs of nephritis, no clinical or serological indications of syphilis.

*Diagnoses.*—Aortic regurgitation of rheumatic origin; rheumatic aortitis; angina pectoris (Heberden); arteriolar hypertonus.

*Subsequent Course.*—After a prolonged period of observation, covering many attacks, all who saw the patient became convinced that she suffered from genuine angina pectoris. The seizures were precipitated by exertion, excitement, or exposure to heat or cold, and were always accompained by severe angor animi. The pain began in the precordia or left side of the neck, and radiated up the neck, down the left arm, and throughout the whole left chest. The blood pressure did not rise appreciably. Nitrites always gave prompt relief. The number of paroxysms was reduced considerably by continuous administration of moderate doses of euphyllin and tincture of digitalis.

A year later (August, 1929) the patient was re-examined and her condition found to be essentially unchanged. She had reduced her weight to 165 lb. The intervals between anginal seizures were averaging three or four weeks in length. The electrocardiogram remained as before.

In October, 1930, the patient's weight was about 155 lb., and she was somewhat more active. The maximum inter-anginal interval was six weeks. Digitalis and euphyllin continued to be absolutely essential to her comfort.

## COMMENT

This case illustrates again the old observation, recently re-emphasized by White and Mudd, that Heberden's angina pectoris in young persons seems to be related definitely to rheumatic aortic regurgitation. In addition, in presenting more than merely inferential evidence of rheumatic aortitis, it calls particular attention to the possibility that rheumatic infection of the root of the aorta plays an important etiological rôle in the angina pectoris of the young.

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# SURGICAL ARTERIOVENOUS ANEURYSM IN THE TREATMENT OF THORACIC ANEURYSM

## A Case Report

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IN 1926 Babcock[1] presented a patient upon whom he operated for the cure of a thoracic aneurysm. The operation was based upon the principle that by increasing the velocity of blood passing through the aneurysmal sac, the intravascular tension will be diminished. This was attained by making an end-to-end anastomosis between the common carotid artery and the internal jugular vein. In effect, the operation produces a large leak from the aneurysm back to the right heart.

This is in accord with the simple hydrodynamic law that a liquid moving through a tube under pressure exerts pressure against the wall of the tube inversely as the velocity of flow through the tube. A reduction of resistance causes an increase in the velocity of the blood through the sac, resulting in a reduction of the lateral pressure on the walls of the aneurysm, thereby lessening the tendency of the aneurysm to burst.

The patient that he operated upon was in a sufficiently precarious condition to warrant the employment of such a radical procedure. After a stormy postoperative course the patient rapidly improved and was able to return to work.

X-ray studies showed a definite decrease in the size of the aneurysm and a slight increase in the size of the heart.

At Mount Sinai Hospital a similar patient presented himself in imminent danger of rupture and death. The same operation was considered, but it was felt that the patient was too poor a surgical risk. It was decided to perform a side-to-side anastomosis between the brachial artery and vein in an attempt to reduce the intra-aneurysmal pressure. A study of the case will show that the result of the operation was not in accord with expectations.

In 1923 Lewis and Drury[2] showed clinically in five cases of arteriovenous aneurysm resulting from war injuries and experimentally after operations on dogs that arteriovenous aneurysm or side-to-side anastomosis resulted in a lowering of the diastolic pressure, a water-hammer pulse with a collapsing quality, an increase in the blood pressure in the leg (Hall and Rowland sign of differential blood pressures in the arm and leg), capillary pulsation, increased heart rate, and enlargement of the heart; these signs in other words represented the hydrodynamic phenomena of aortic regurgitation. Gage and Herrmann[3] confirmed these observations.

## CASE REPORT

J. M. P., aged fifty-two years, seaman-painter, was admitted to the Mount Sinai Hospital, New York, on April 10, 1928, complaining of a painful lump of two months' duration on the anterior chest wall. He had been married for eight years, and his wife had never been pregnant. He admitted having had a chancre on the penis twenty years before, and had received local and general treatment at that time. He had been subject to pains in the anterior chest radiating to the right scapula and arm for two years. The pains were intermittent and lasted only from three to five days at a time. They had decreased in severity until two months before admission, when he had a sudden severe pain in the same location; the pain disappeared as suddenly. In twenty-four hours he noticed a lump protruding from the anterior chest wall. Since then the pain had been less, but the mass had increased in size. The mass showed pulsation, which increased in intensity, and lately increased pain was noted.

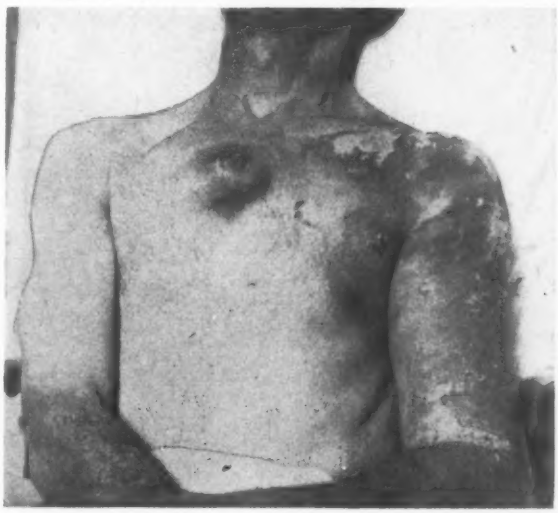

Fig. 1.—Photograph showing the aneurysm on the anterior chest wall and the swelling of the left arm two weeks after operation.

The physical examination revealed irregular, unequal pupils, which did not react to light; an expansile mass on the anterior chest wall, 8 cm. in diameter and 4 cm. in height, just to the right of the sternum. The heart was enlarged to the left and downward, and the mediastinal dullness was widened on percussion. At the apex the sounds were distinct and there was a systolic murmur. At the aortic area the second sound was present and there was no diastolic murmur. Over the aneurysm there was a low pitched systolic and diastolic bruit. The systolic bruit was transmitted to the vessels of the neck. There were no signs of aortic insufficiency. The fundi were normal. The blood Wassermann test was four plus. The uranalysis was normal, and the blood count showed hemoglobin of 80 per cent, white blood cells 10,500 per cmm., polymorphonuclears 49 per cent, eosinophiles 1 per cent, lymphocytes 48 per cent, and mononuclears 2 per cent.

Within two weeks the mass had increased in size and measured 10.5 cm. in diameter and 5.5 cm. in height. Direct arteriovenous anastomosis between the common carotid artery and the internal jugular vein on the right side was considered but dismissed in favor of the side-to-side anastomosis between the left

brachial artery and vein. This was done in the usual method by Dr. Edwin Beer. When the operation was completed, the vein gradually dilated under observation and the radial pulse remained palpable. The superficial veins distal to the anastomosis became dilated and remained engorged. The blood pressure taken in the leg dropped from 120/60 mm. before operation to 120/30 mm. after operation. In the arm the blood pressure dropped from 145/95 mm. to 120/55 mm. These readings were taken at different times.

The immediate postoperative result was freedom from pain. The veins in the antecubital fossa became more distended. The aneurysmal mass appeared to increase in size. Two weeks after the operation, the patient began to complain of pain at the site of the operation, where there appeared an area of brawny induration. This extended down the left arm, and remained for one week. The radial pulses were equal, and the bruit over the site of the anastomosis persisted. Wet dressings were used in the treatment of this condition, which was probably due either to a phlebitis or to mechanical obstruction to the return flow of the blood.

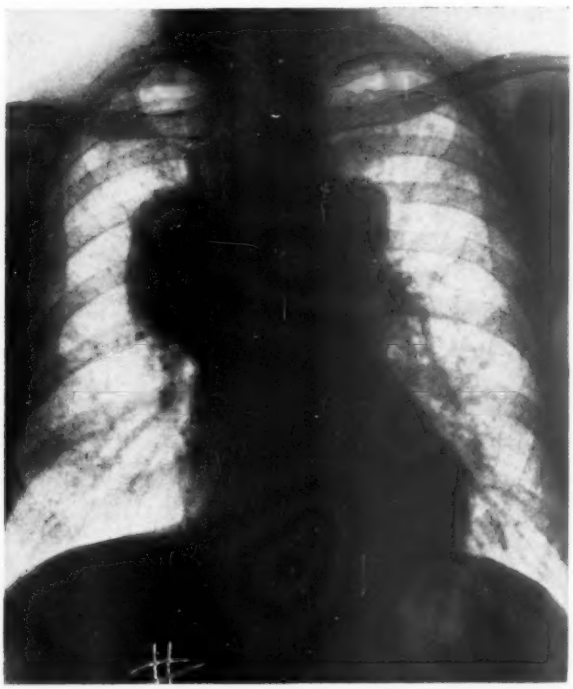

Fig. 2.—Teleroentgenogram of chest.

The electrocardiographic tracing before operation showed a slight thickening of the QRS complex in Lead III, but no other abnormality. After operation, no abnormality was found.

The teleroentgenogram showed a saccular aneurysm involving the ascending arch of the aorta, and four weeks after the operation a slight increase in the size of the aneurysm was noted.

The patient was discharged apparently improved but returned in ten days with the mass somewhat larger protruding from the anterior chest wall. The superficial

skin was ulcerated, and bright red blood was oozing from the eroded areas. The next morning the patient suddenly began to bleed profusely, became exsanguinated and died.

The post-mortem report revealed that beneath the defect in the skin and sternum as well as the second left costal cartilage, lay the aneurysm occupying the first portion of the aorta, with a perforation, 2 cm. in diameter, covered by a blood clot. There was a second smaller aneurysm to the right of the first. There were also present a luetic aortitis and an acute splenic tumor. The anastomosis between the left brachial artery and vein was patent.

BLOOD PRESSURES BEFORE OPERATION

| DATE | LEFT | RIGHT | |
|---|---|---|---|
| April 10, 1928 | 140/80 | 135/75 | |
| 19, | | 140/90 | |
| 22, | | 145/95 | |
| 10 P.M. | 120/60 (leg) | | |
| AFTER OPERATION—APRIL 22, 1928 | | | |
| 11 P.M. | 120/32 | | |
| 12 Noon | 110/30 | | |
| 23, | 120/60 | 115/55 | |
| 24, | | 120/60 | |
| 26, | | 106/58 | |
| 27, | | 116/60 | |
| 29, | 102/48 | 104/50 | |
| 30, | 116/65 | 116/60 | |
| June 13, | 126/72 | 118/68 | before exsanguination |

## COMMENT

In the case reported the operation performed served to add the further embarrassment of the hydrodynamics of an aortic insufficiency to a circulation already embarrassed by an aneurysm.

The Babcock operation has possible merit in that it is based on a sound hydrodynamic principle. The hydraulic effect of an end-to-end union is entirely different from that of a side-to-side communication in the treatment of thoracic aneurysm. This is borne out clinically in the case presented.

It is obvious that no hard and fast conclusions can be drawn from the report of this case, except that the formation of an arteriovenous aneurysm to relieve the lateral pressure on the walls of a thoracic aneurysm was of no avail.

This case report is presented through the courtesy of Dr. George Baehr of the Second Medical Service and Dr. Edwin Beer of the Second Surgical Service of the Mount Sinai Hospital of New York.

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# Department of Reviews and Abstracts

## Selected Abstracts

**Levine, Samuel A., Andren, Thekla, and Homans, Katharine A.: Nosebleed and Vomiting in Rheumatic Individuals.** New England J. Med. 203: 832, 1930.

The frequency of spells of nausea, vomiting, and epistaxis was ascertained in one hundred individuals suffering from rheumatic fever or one of its allied conditions like chorea or rheumatic heart disease. This was compared with the frequency with similar symptoms in a control group of one hundred nonrheumatic individuals of approximately the same age coming to a surgical clinic. According to the method used in estimating the occurrence of these symptoms they were found to be three to four times as frequent in the rheumatic as in the nonrheumatic group. The authors believe that attacks of inexplicable nausea and vomiting and spontaneous nosebleed are in some way related to the rheumatic infection. They occur frequently during a period of the infection that generally is regarded as inactive. Epistaxis particularly may occur for years preceding the first definite attack of rheumatism. These features, together with others more commonly emphasized, will enable the physician to identify as rheumatic many conditions which at present go unrecognized or misdiagnosed.

**Shoemaker, Robert, III, and Eckels, John C.: Bullet in the Heart.** New England J. Med. 203: 195, 1930.

A white woman twenty-three years old was brought into the hospital with two bullet wounds in her chest. One bullet was found localized in the chest wall and under local anesthesia a 22-caliber bullet was removed in the situation indicated by the x-ray report. The other bullet was localized apparently in the wall of the ventricle on the anterior surface probably in the right side. It showed an excursion of 2 cm. during the cardiac cycle. It was decided that since the patient was recovering after emergency shock treatment that no attempt should be made to remove this foreign body. Physical examination otherwise was unimportant. Electrocardiograms made during convalescence showed a normal cardiac rhythm. The patient recovered, was discharged at four- and eight-week intervals for reexamination.

**Fitzhugh, Greene: A Clinical and Pathological Study of Chronic Myocarditis.** New England J. Med. 203: 201, 1930.

An analysis of the clinical and pathological records of 228 selected fatal cases was undertaken to study the relation between the clinical syndrome and the necropsy findings in cases of cardiac failure. Cases chosen for study were those in which the heart showed at necropsy hypertrophy and dilatation, fibrosis, or infarction of the myocardium. Hearts with valvular lesions were not included. All of these except 28 showed during life clinical evidences of myocardial insufficiency. Of the 228 cases, 125 died of cardiac failure and form the cardiac group. Fifty-five died of nephritis, 14 of cerebral hemorrhage, and 34 of miscellaneous causes, making up the noncardiac group. The author then proceeds to analyze the various an-

atomical lesions found at necropsy and also the usual symptoms shown during life in these two groups of patients. Importance of such studies as this cannot be overemphasized in throwing light on the significance of various clinical symptoms.

**Hoskin, Jenner: The Effect of Auricular Fibrillation on the Operative Risk in Hyperthyroidism.** Brit. M. J. July 26, p. 138, 1930.

The present paper is the result of an investigation of 356 consecutive cases of Graves' disease, exophthalmic and toxic, in which all but 4 had operative treatment; 315 were cases of exophthalmic goiter and 41 of toxic goiter. Thirty cases of auricular fibrillation were found, 22 among the exophthalmic goiter cases and 8 among the toxic, a total of 9.52 per cent. It is probable that a few cases of transient fibrillation may have been overlooked.

There were 12 transient cases, of which 10 occurred after partial thyroidectomy; in the remainder, paroxysmal attacks of auricular fibrillation were noted electrocardiographically prior to operative treatment. In all 12 cases normal rhythm was reestablished within a week of the operation without quinidine being administered. Of the 18 cases of permanent fibrillation, there were 4 deaths, 3 following operation. Of the remaining 14 cases 7 became normal within a few days of operation, and in 7 the irregularity persisted. Of these 7, three were not operated upon, 3 had partial thyroidectomy performed, and in 1 case the superior thyroid vessels were tied. One of these cases in which normal rhythm was restored by partial thyroidectomy relapsed into auricular fibrillation four months later.

Out of the 356 cases investigated, the total mortality was 20. The presence of auricular fibrillation must be regarded as a distinctly unfavorable complication during operation. It is associated with cardiac enlargement, rapid pulse rate, and signs of congestive failure. The effect of the toxic thyroid secretion as shown by the raised basal metabolic rate is aggravated by an added impairment of cardiac function caused by the congestive failure. It is essential, therefore, that the thyrotoxicosis should be reduced and the ventricular rate controlled before operative procedure is contemplated. Lugol's solution in combination with digitalis is indicated in preparing these patients for operation.

**Willner, Otto: Some Observations on Mitral Stenosis and Measurements of Normals Among Chinese.** Am. J. M. Sc. **180:** 200, 1930.

Among 24,000 patients admitted to the Peiping Union Medical College Hospital during seven and one-half years, 95 men and 62 women were found to have mitral stenosis as a single or combined valvular lesion. It would seem that there is a low incidence of typical rheumatic fever among these people. In this group of patients it was found that the asthenic habitus was prevalent.

For comparison an examination was made of 150 healthy young Chinese adults in order to determine whether there was a correlation between the 3 predominating characteristics found in the group of individuals with mitral stenosis, namely, asthenic build, mitral configuration of the heart, and a large angle of the electrical axis. It was not clear that such a correlation existed.

**Parsonnet, Aaron E., and Hyman, Albert S.: Barium Chlorid in the Stokes-Adams Syndrome of Complete Heart-Block: Negative Results in Eight Cases.** Am. J. M. Sc., **180:** 356, 1930.

The authors have been interested in the use of barium in a series of eight cases of complete heart-block complicated by the Stokes-Adams syndrome. In none of these cases were they able to obtain any semblance of pharmacological or physiological action either good or bad. Special attention was focused upon the quality and the source of barium employed. Amounts varying from 0.04 to as much as

0.6 gram were given in twenty-four hours; these doses were continued in various cases from one week to three months, and electrocardiographic control of each case was made from every two weeks to two months. While this series of eight cases is not large, the authors point out that the Stokes-Adams syndrome is by no means common and that the series is extensive enough to challenge the test of barium efficacy.

**Harvey, Earle A., and Levine, Samuel A.: A Study of Uninfected Mural Thrombi of the Heart.** Am. J. M. Sc. **180:** 365, 1930.

A study was made of all the necropsy protocols at the Peter Bent Brigham Hospital for the interval 1913-1929 in which 2,091 records were reviewed. The incidence of thrombi of the heart in patients coming to necropsy was found to be approximately 5.3 per cent or 111 instances. Seventy-three occurred in males and 38 in females. The thrombi were noted most frequently in the later years of life. The two decades from fifty to sixty-nine included more than half of all the cases. A positive Wassermann was noted in about 10 per cent, which is about the average incidence in all cases coming to the hospital. The frequency of sites of formation of single thrombi were: left ventricle 31, right auricle 28, left auricle 6, right ventricle 4. There were 42 cases of multiple thrombosis. The apices of the ventricles and auricle appendages were the most frequent sites of formation of mural thrombi. Auricular fibrillation definitely increases the incidence of auricular thrombosis.

The authors believe from their study that the two most frequent mechanisms for the formation of cardiac mural thrombi are the myocardial degeneration associated with coronary arterial disease and the improper functioning of the auricles leading to blood stasis. The diagnosis of cardiac mural thrombi rarely is made during life but should be suspected in cases of coronary thrombosis and coronary valvular disease showing evidence of emboli.

**Niles, Walter L., and Wyckoff, John: Studies Concerning Digitalis Therapy in Lobar Pneumonia.** Am. J. M. Sc. **180:** 348, 1930.

This study is an attempt to determine the effect of digitalis as a therapeutic measure in the care of patients with lobar pneumonia. The number of cases available for the study has been sufficiently large to warrant drawing conclusions of value. The study has been conducted over a period of at least two years' time on patients admitted to the hospital with lobar pneumonia under carefully controlled conditions and given digitalis in sufficient amounts to produce clinical effects. Results of this study should be known to every clinician, since it marks a most important contribution to the subject.

It would seem that patients with pneumonia are not benefited by digitalis therapy; in fact, in this series of cases the mortality was slightly higher in the group of patients who were digitalized than in those who received none.

Numerous tables analyze results from several standpoints. From a study of the tables it would seem that for every one hundred cases in the control group who died there were one hundred and twenty-two fatalities in the digitalis treated group. In a small group of patients receiving a preparation of digitalis with higher potency than indicated the mortality was 13.5 per cent higher than of the control group, or at the rate of 140 patients for every 100 control patients. The mortality rate is higher for both sexes in the digitalis treated groups as compared with that of the controls. Tables also show that the mortality of the digitalis treated cases is higher than that of the corresponding controls in both the older and younger groups. It is also shown that in all types of pneumonia, except type

II, the mortality of the digitalis treated cases is higher than that of their controls. The only exception to this is that the higher mortality in the digitalis treated cases is found in the younger age group with type II pneumococcus infection. No explanation has been found for this exception. Possibly the factor of virulence in producing septic complications may determine it. The last table shows that the incidence of auricular fibrillation and auricular flutter is the same in the control and the digitalis treated group. The mortality is, however, distinctly higher in the digitalis treated group.

In conclusion, the Committee prefers to continue this investigation on the results of digitalis therapy in pneumonia and to observe a larger number of cases over a series of years. It was the unanimous opinion of the Committee and its advisers that the results obtained thus far do not justify continuing the routine administration of digitalis to patients suffering with lobar pneumonia.

**King, Frances W., and Hansen, Olga S.: Electrocardiographic and Roentgenographic Studies of the Heart in Tuberculosis.** Am. Rev. Tuber. **22:** 310, 1930.

Studies of electrocardiograms and x-ray plates have been made on one hundred unselected cases of tuberculosis at Glen Lake Sanatorium. The diameter of the heart was found to be lower in this series than in normal individuals. The hearts of one hundred cases without hypertension or heart disease coming to autopsy showed that the weight of the heart in this series is on the whole lower than that in the nontuberculous. Nearly one-third of this group had a cardiothoracic index below 40 per cent as compared with one-fifth in the normal.

The electrocardiograms of this group of patients following collapse therapy revealed that a high percentage (60 per cent) showed low voltage in one or more leads, the amplitude of the ventricular complex measuring not more than 5 mm. Roentgen ray studies indicated that the heart shadow was displaced by tuberculous processes in a considerable number of cases. Study of electrocardiograms in these cases with displacement of the heart shadow yields insignificant results. The incidence of low voltage is practically the same in the right-sided heart and in the normally placed heart. The infrequent occurrence of low voltage in Lead I in the presence of left heart displacement is the only point worthy of note in these figures.

**Hansen, Olga S., and King, Frances W.: The Influence of Pulmonary Collapse on the Electrocardiogram.** Am. Rev. Tubere. **22:** 320, 1930.

Electrocardiograms have been studied in sixty-six patients who have undergone seventy-three pulmonary collapse procedures, analyzing findings before and after collapse. These procedures are almost invariably followed by changes in amplitude of the electrocardiographic waves, R-wave modification occurring in 96 per cent of the cases, but the type and the degree of variation are not constant or predictable, according to either the side involved or the procedure carried on.

Evidence suggests that the changes are due to changes in heart position, influenced largely by pleural and mediastinal adhesions, more than by myocardial factors.

**Hitchock, C. H., McEwen, Currier, and Swift, Homer F.: Antistreptococcus Serum Treatment of Patients with Rheumatic Fever.** Am. J. M. Sc. **180:** 497, 1930.

The authors have observed the therapeutic effects of antistreptococcus serum on a group of patients in the hospital for the Rockefeller Institute with rheumatic fever. Three types of serum were used: (1) an antihemolytic streptococcus serum; (2) SCA (indifferent streptococcus) serum, both bovine and equine, and (3) an

anti-green streptococcus serum. The reactions following the use of any one of these three types of serum were irregular and while at times severe, were generally mild and produced no injury to the patient. No well-defined improvements could be observed following the use of sera.

The authors point out that it is not to be expected that any marked specific beneficial action would follow antistreptococcus serum therapy in rheumatic fever, for the disease is not of the general type which would respond favorably to a serum. It is not an acute disease like diphtheria, tetanus or scarlet fever but a subacute or chronic infection resembling tuberculosis or syphilis in many of its features. The amount of material responsible for the various manifestations of the disease which are elaborated and conveyed to the blood varies in amount and intensity over long periods of time.

The authors conclude that antistreptococcus serum in no way should replace the long established therapy of rheumatic fever and that it does not apparently add enough to warrant its universal adoption. In their experiments the unpleasant reactions sometimes attendant upon its application have not been outbalanced by a reciprocal certainty of therapeutic benefit.

**Leech, Clifton B.: Streptococcus Viridans Endocarditis in Children.** Am. J. M. Sc. **180:** 621, 1930.

The records of the Harriet Lane Home revealed 13 instances of streptococcus viridans endocarditis proved by blood culture or by autopsy, 2 unproved but highly probable cases and 1 streptococcus viridans septicemia without endocarditis. The 15 cases represent an incidence of approximately 0.1 per cent. An analysis of these records is partially indicated in the accompanying table. A discussion of the symptoms and signs indicates that this infection produces a clear clinical picture of sufficiently constant characteristics to permit diagnosis even without culture of the blood.

**Fishberg, Arthur M.: Auricular Fibrillation and Flutter in Metastatic Growths of the Right Auricle.** Am. J. M. Sc. **180:** 629, 1, 1930.

Three cases are described in which secondary malignant growths in the right auricle were accompanied by auricular fibrillation or flutter. In the first of these cases the involvement of the right auricle by the tumor was suspected during life; in the two succeeding cases this diagnosis was considered very probable.

**Sheldon, Wilfrid: Rheumatism in Childhood.** Lancet **11:** 394, 1930.

This paper is based on the notes of six hundred consecutive cases of rheumatism seen during the last two years at the Rheumatic Clinic of the Hospital for Sick Children, Great Ormond Street. The children were divided into the following four groups.

One group was of 235 children with rheumatic pains in the limbs. These children form an important group, because of the possibility of a later development of heart disease. The pains rarely develop before the age of three years. They are especially frequent during the night, and they occur in many parts of the body, chiefly the legs. An accompanying curve shows that the pains occur more frequently during the seasons when there is greater rainfall. Fifty-two of 266 children with rheumatic heart disease complained of these pains as the only symptoms preceding the discovery of the heart disease; similarly 15 children out of 197 cases of chorea gave a history of such pains in the limbs.

The second group was of 133 children with a history of rheumatic fever or acute articular rheumatism. These children are rarely seen before the age of three years. The author describes the well-known characteristics of rheumatic fever in young children. He believes that the relationship between rheumatic fever and heart disease is well recognized. In this group, 93 children (70 per cent) showed evidence afterward of cardiac involvement; of the remainder, the rheumatic fever was followed by chorea in 5 cases. Only 23 children had been entirely free of rheumatic symptoms since their attack of rheumatic fever.

The third group was of 197 children with chorea. Of this group, rheumatic heart disease occurred in 52; rheumatic fever preceded the chorea in 5 cases, and in 15 instances rheumatic pains in the limbs either accompanied or followed the chorea. Children with chorea are apt to be quick and intelligent and keen on their school work.

The fourth group was of 266 children with rheumatic heart disease, a percentage of 44. The author discusses the early diagnosis of the heart disease, particularly the differentiation of murmurs associated with organic valvular lesions and functional disturbances. Aortic regurgitation was present in 6 per cent of this group of children.

The question of tonsillectomy in children with rheumatism is discussed briefly. In this group of children tonsillectomy has been performed on 90 per cent. Three hundred ninety-three were operated on before admission to the clinic. Cases in which visible tonsil remnant remained after the operation have not been included in this study. Approximately one-third of the cases of rheumatic pains, chorea, and rheumatic fever begin these symptoms of rheumatic infection after the tonsils have been removed. The author believes that unless it can be shown that tonsillectomy has a definite influence in the prevention of cardiac disease there seems small justification for the operation merely on the ground that the child is a rheumatic suspect. It seems more probable that the value of tonsillectomy in rheumatic children is in proportion to the degree of impairment of the general health attributable to the tonsils.

**Buffum, William P.: Management of Convalescence in Rheumatic Heart Disease.** Rhode Island M. J. **13**: 127, 1930.

The author discusses the many criteria that can be used in watching individuals convalescent from active rheumatic fever and heart disease. Usual points to be noted are the temperature, pulse rate, general appearance, and color of the child, weight curve, and the physical signs noted on examination of the heart. Furthermore, subcutaneous nodules should be looked for; the leucocyte count should be followed, and occasionally the determination of vital capacity may serve as a guide to satisfactory progress. The vital capacity can be used as an index of the functional capacity of the heart.

He points out that the determination of whether or not the active disease has ceased is at times very difficult and that it is not possible to rely entirely on any one of the above signs. During further convalescence, after the patient is up, any recurrence of these signs of active disease shows that the patient should be put to bed again.

The author makes the important statement that in general it is better to consider the child as a whole rather than to focus the attention too much on the heart. He discusses the regulation of exercise and the general care that should be provided these patients. He also discusses the value of tonsillectomy in the control of further attacks of rheumatic fever.

**Smith, Arthur L.: Configuration of the Heart in Cardiac Disease.** Neb. State M. J. **15**: 337, 1930.

The author points out that accurate diagnosis of heart disease depends upon careful history taking, complete physical examination, and laboratory findings combined with employment of sensitive scientific instruments and exacting interpretation of the findings. No one method will suffice for an accurate diagnosis.

He believes that there is no such thing as x-ray diagnosis of heart disease. The size, shape, and position of the heart vary greatly in a normal person, and if these alone are considered, the diagnosis will often be incorrect. He describes the usual appearance of the heart in roentgen ray films and also describes the changes that occur as the result of valvular disease and muscle enlargement. He believes that each condition affects the appearance of the heart picture in a characteristic way.

**Drake, Carl B.: The Clinical Aspects of Sclerotic Changes in the Aortic Valve.** Minn. Med. **13**: 628, 1930.

Four cases are reported in which there was thickening with calcification in the aortic valves with physical signs suggestive of aortic stenosis. The author points out that the lesions may arise in old healed rheumatic valvular endocarditis. He believes that the aortic stenosis is the predominating lesion produced by the sclerosis but that there may be in many instances also an accompanying aortic insufficiency. Physical signs of aortic insufficiency may be obscured by those of the stenosis.

The sclerotic process producing aortic stenosis does not particularly shorten life, is a gradually progressive affair, and the patient usually adapts himself to a definite limitation in the field of his cardiac response.

**McKinlay, C. A.: Valvular Heart Disease in Young Adults.** Minn. Med. **13**: 624, 1930.

The observations noted in this paper are from 67 cases, chiefly university students who were found on entrance and subsequent physical examination to have valvular heart defects. They represent a selected group without cardiac decompensation who had suffered little or no inconvenience from their condition.

A relatively high incidence of aortic insufficiency was noted in the series. Clean tonsillectomy had been done in only about one-half of the cases. Frequency of hypertrophic and follicular pharyngitis is discussed in view of possible significance in relation to rheumatic fever, the methods of treatment and prevention.

**Jolliffe, Norman: Liver Function in Congestive Heart Failure.** J. Clin. Investigation **8**: 419, 1930.

The frequency of clinical jaundice in a series of 231 patients with congestive heart failure was observed to be 2.1 per cent. The jaundice in this type of failure may be of either the obstructive or the nonobstructive type. Using various methods to study liver function, 15 of the 16 patients had some alteration in liver function, though no characteristic type was found. Three subjects showed only one abnormal response to liver function tests; only one subject showed all tests abnormal.

No parallelism between degree of heart failure and impairment of liver function could be noted in individual cases. As a group there was perhaps a parallel between the changes in liver function and the degree of edema and size of the liver. Any liver dysfunction induced by an attack of chronic passive congestion is apparently not permanent. Liver dysfunction still in evidence after recovery from an attack of chronic passive congestion indicates an independent liver impairment.

**Bock, A. V., Dill, D. B., and Edwards, H. T.: On the Relation of Changes in Blood Velocity and Volume Flow of Blood to Change of Posture.** J. Clin. Investigation **8**: 533, 1930.

Estimations of the circulation time as measured by reaction to histamine indicate a retardation of the velocity of blood flow in the standing position in man. The authors believe this fact supports previous experimental evidence showing a reduction of the total output of the heart when the subject stands still.

**Pardee, Harold E. B.: The Significance of an Electrocardiogram with a Large Q-wave in Lead III.** Arch. Int. Med. **46**: 470, 1930.

Attention is directed to the occurrence of records showing left axis deviation of QRS or a normal electrical axis, combined with a large Q-wave in Lead III, one that is 25 per cent or more of the largest deflection of QRS in whichever lead this may occur.

The majority of such records are obtained from patients with the anginal syndrome, but certain patients with myocardial fibrosis and congestive failure, certain patients with rheumatic heart disease, especially with pericarditis, and a few with hypertension will give such records. Certain patients who have cardiac symptoms but no definite evidence of cardiac disease have been found to show this large Q-III, and rarely (twice in 277 cases) such records are obtained from apparently normal hearts.

These records show a clockwise rotation of the vectors of the QRS group, and frequently there is an inversion of T-III or of T-II and T-III. Both of these features depend on right ventricular activity, and it is suggested that the finding of a large Q-III indicates disease of the left ventricle, so that the right ventricle predominates during the spreading of the contraction in spite of the left axis deviation or normal axis direction of QRS. The effect of diaphragmatic movements on the large Q-III is noted and it is suggested that the occasional finding of a large Q-III in normal hearts may be due to an unusual distribution of the branches of the A-V bundle and that a high position of the diaphragm may be a contributory factor.

**Nyiri, William, and DuBois, Louis: Experimental Studies on Heart Tonics. IV. The Main Factors of Digitalis Standardization with a New Assay Method.** J. Pharmacol. & Exper. Therap. **40**: 373, 1930.

The authors believe that warm-blooded animals are to be preferred as test material to animals lower in the animal scale and to plants. They also believe that the best way of administering heart tonics in the assay is the intravenous injection. Intravenous anesthesia is also to be preferred to the former methods of narcosis in animal experimentation in general and for the standardization of heart tonics in particular.

The fall of blood pressure to zero, approaches closest the theoretically expected end point of the experiment and thus is to be preferred to the observation of the stoppage of the heart and the general death of the animal.

Based on the study of these principal factors a practical method of digitalis standardization is described using the rabbit as test animal. This method has the following advantages: the animal is always easily available. The end point of the assay obtained by means of the drop of the blood pressure, supplementing the test of the use of ouabain, is definite and as close to the theoretical end point as may be expected. Because of the higher resistance to digitalis the method allows the testing of drugs of high concentration as well as drugs of great dilution without preliminary injurious manipulations of the heart tonics.

All methods of standardization of heart tonics, including the one herein described, are toxicity tests and use the death of the heart or of the entire organism as final criterion. In view of the therapeutic purpose of the heart tonics any method dealing with the determination of the therapeutic efficiency instead of the fatal dose obviously would be preferable. Unfortunately, such a method is not available at present.

**Dawson, M. H., and Boots, R. H.: Subcutaneous Nodules in Rheumatoid (Chronic Infectious) Arthritis.** J. A. M. A. **95:** 1894, 1930.

The authors have found a relatively high—approximately 20 per cent—incidence of patients with subcutaneous nodules in a group of approximately 200 individuals suffering with true rheumatoid arthritis. The nodules have been observed only in cases of typical rheumatoid arthritis, and in one case of Still's disease. Three of the patients in whom the nodules occurred presented a history of a previous attack of rheumatic fever; four patients showed definite evidence of rheumatic heart involvement; in one patient the development of arthritis and the appearance of nodules appeared to bear a definite relationship to a previous attack of scarlet fever.

Nodules have been excised from 14 patients and subjected to careful histological and bacteriological examination. The material examined showed a striking uniform and characteristic picture.

This study sustains the following conclusions: The subcutaneous nodule occurring in rheumatoid arthritis is a classic lesion of this disease. The histologic appearance of these nodules is uniform and highly characteristic. There is a striking histologic resemblance between the subcutaneous nodules occurring in rheumatic fever and those observed in rheumatoid arthritis.

**Sprague, Howard B., and Graybiel, Ashton: Salyrgan as a Diuretic. Report of Sixty Cases.** New England J. Med. **204:** 154, 1931.

Sixty cases treated with salyrgan are reported. Forty-six patients had cardiac diseases with digestive failure; eight had cirrhosis of the liver; four had cancer; and one each nephrosis and ovarian cyst. Diuresis was secured in 80 per cent of the cases and in 55 per cent this diuresis exceeded twice the fluid intake. The diuretic effect may often be increased by the use of ammonium chloride or nitrate.

The authors feel that the drug is an active and safe diuretic of particular value in the treatment of congestive heart failure with edema of ascites from various causes, and of nephrosis. It should be used early in the therapy of these conditions and not reserved as a drug of last resort.

The toxic effects from Salyrgan are very rare and consist of mild renal, gastrointestinal or skin irritation.

This work supports the view that the chief effect of mercurial diuretics is directly upon the kidney.

**Wolferth, Charles C., and Margolies, Alexander: The Influence of Auricular Contraction on the First Heart Sound and the Radial Pulse.** Arch. Int. Med. **46:** 1048, 1930.

A series of 7 cases with varying auriculoventricular relationships all showed inequalities of the first heart sound which could be related to the lengths of the intervals between auricular and ventricular systoles. These time relations tended to be characteristic for each case, although the degree of inequality varied and exceptionally could not be recorded.

The inequalities of sound are usually detected by auscultation and furnish a valuable clinical test of dissociated beating of the auricles and ventricles. The absence of inequality of sound does not rule out the possibility of dissociated beating. In two cases inequalities in the size of the pulse waves were recorded. When the amplitude of the waves recorded was compared with the lengths of intervals between auricular and ventricular systoles, a definite relation was revealed. In both cases the curves showed similar time relations. In one, inequalities in amplitude seemed to vary from day to day, and occasionally no differences could be recorded. In three other cases tracings of the pulse waves failed to reveal changes in the amplitude of the waves that could be related to the auriculoventricular intervals.

Simultaneous records of changes in the intensity of sound and amplitude of the pulse waves showed that comparatively loud or faint sounds may be associated with comparatively large or small pulse waves. It was, therefore, concluded that while both types of changes were dependent on phenomena resulting from auricular systole, the factors concerned were not identical.

It is suggested, by indirect evidence obtained in this study that the changes observed in the amplitude of the pulse waves are due principally to the effects of auricular systole on ventricular filling and initial tension. The provisional hypothesis is adopted that inequalities of the first heart sound observed are due principally to variation in the position of the mitral leaflets at the beginning of ventricular contraction.

The data presented indicate that in the clinical evaluation of the first heart sound as evidence of cardiac vigor, modifications dependent on the duration of the auriculoventricular interval should be discounted.

**Drinker, Cecil K., and Field, Madeleine E.: Absorption From the Pericardial Cavity.** J. Exper. Med. **53:** 143, 1931.

The pericardium in the rabbit proved to be a singularly inert protective membrane. Simple solutions placed within the sac are held without leakage and are absorbed practically entirely by the subepicardial blood capillaries. Such solutions do not leak through the extraordinarily thin pericardial membrane into the pleural cavities even if subjected to slight pressure. When substances such as serum or graphite are injected, removal is extraordinarily slow. No evidence was obtained from the study showing the abrupt direct type of lymphatic entrance which is seen in the central tendon of the diaphragm after intraperitoneal injections. Such lymph drainage as occurs is through lymphatics in the pericardium around the base of the heart and to a slight extent along lines of fat deposition in the pericardium. The subepicardial lymphatics are entered with great difficulty from the pericardial sac, a condition favorable to exclusion of the heart from participation in pericardial infections.

# Book Reviews

La Pratique Médicale Illustrée. Les Endocardites Infectieuses—Diagnostic—Traitement. Directeurs Professeur E. Sergent, R. Mignot, R. Turpin. Par A. Lemierre and P. M. Deschamps. Paris, 1930, G. Doin & Cie.

This is one of the series of fasciculi on various branches of clinical medicine published under the direction of Professor Sergent in Paris. Any publication bearing the signature of Lemierre is worthy of careful study, and this volume is no exception to the rule. Some forty years ago that admirable clinician Neusser, of Vienna, sent one of his assistants to study in Paris with the observation: "The French excel in symptomatology." There are indeed no clearer clinical descriptions than those of the better French clinicians, a truth to which this brochure testifies.

In the preamble the authors observe: "From a very general point of view the infectious endocarditides present themselves to the physician under two different circumstances. On the one hand, in the course of a given infection, they may constitute a complication which should be systematically sought for because we know it to be very common under such conditions, but which remains in the background and exerts no influence on the immediate prognosis; this is the situation which is generally met with in the course of acute articular rheumatism where Bouillaud's laws should always be in one's mind. On the other hand, the endocarditic complication may overshadow the other manifestations of the disease which gives it birth: it dominates the prognosis. So it is in certain malignant rheumatisms and in the greater part of the so-called ulcero-vegetative endocarditides." They accordingly consider infectious endocarditis under two headings: (1) Rheumatic endocarditis which, anatomically, is verrucose or plastic. (2) Infective endocarditis proper, malignant or septic endocarditis dependent on infection with pyogenic organisms and characterized anatomically by ulcerative and vegetative processes.

Rheumatic endocarditis they divide into (1) *Simple rheumatic endocarditis* and (2) *Malignant septic endocarditis.*

The insidious origin and course of the ordinary rheumatic endocarditis are well described and contrasted with the clinical picture of rapidly progressive rheumatic pancarditis with early cardiac failure. The differential diagnosis between acute rheumatic pancarditis and what we call infective or bacterial endocarditis is admirably set forth. They insist, especially, on the predominance of signs of cardiac failure

in the former even if they be associated with symptoms suggesting grave pyogenic infection. They devote eight pages to the careful description of malignant rheumatic endocarditis and its distinction from bacterial endocarditis.

They then take up "the infective malignant or septic endocarditides" dependent upon infection with pyogenic organisms, describing first the acute forms in a general way before taking them up from an etiological standpoint. They point out their differences from malignant rheumatic endocarditis in the existence of a septicemia, ulcero-vegetative lesions and the frequency of embolic phenomena, and they insist, particularly, on the circumstance that the cardiac phenomena remain generally in the background. The outstanding symptoms are those of a septicemia. From a general clinical standpoint they consider cases of a typhoidal aspect with high continued fever, and the pyemic type with irregular remittent and intermittent fever. They call attention to the occasional instances in which the foci of infection are parietal and difficult to recognize clinically, and they refer to that group of cases in which the onset is sudden, with early and repeated embolisms. Finally they acknowledge that one may almost speak of a "cardiac form" with terminal thrombosis of the right side of the heart and pulmonary embolisms.

From an etiological standpoint they discuss *streptococcal, pneumococcal, gonococcal* and *staphylococcal* infections, and then mention rarer forms—endocarditis due to *typhoid bacilli, enterococci* (which we should include under streptococci), *colon bacilli, M. tetragenus* and the pneumobacillus.

On page 30 the reviewer is quoted as having found infection with pneumococcus I more frequent than with the other types. With augmented experience the reviewer has found that among 31 cases the infection has been evenly divided between Types I, II and IV, one case only showing a Type III infection.

The authors then take up *subacute, infective, malignant, endocarditis* which they distinguish from the *infectious malignant endocarditis of a prolonged course* in that its duration is from one to three months only. The description is admirable. At the outset they insist on the frequency with which the process takes its origin on the basis of an old valvular lesion, and that, after all, as Vaquez happily expressed it, "it is, in reality, a manner of death for patients the subject of valvular lesions."

On page 37, in speaking of embolic phenomena, they point out the difference between the clinical evidences of embolisms springing from thrombi in right and left heart. On the same page the remarkable statement is made that subacute endocarditis of the left heart is only observed in chronic mitral disease ("qui ne s'observe guère que chez les mitraux"). This is perhaps a little exaggerated. The reviewer

can put his hand immediately on the records of nineteen instances of infective endocarditis of the left heart of a duration of from one to three months in his own series, in which the aortic valves were involved. In eight of these the mitral valves were unaffected; in three more the mitral involvement appeared to have been coincident with that of the aortic valves, that is to say, purely subacute. In the streptococcal series where the infective focus is more commonly on the seat of a chronic rheumatic lesion there were nine instances of involvement of the aortic valves, in two of which the mitral curtains were normal; in a third, the mitral involvement appeared to have been purely subacute.

They then consider "*Infective malignant endocarditis of slow or prolonged course.*" The manner of origin and the course of the infection are carefully described and the diagnostic features judiciously discussed. Under specific headings are considered (1) the *probable* signs—fever, anemia, splenomegaly, arthralgia—in association with the relative absence of alteration in the patient's general condition and of signs of cardiac insufficiency, and then (2) the *certain* signs, especially embolic. They emphasize the circumstance that the emboli are not generally infective, at least in the sense that they do not, as a rule, result in abscesses, but produce mainly mechanical effects. This, in a general way, is true, but it is only relatively so, for one should remember the frequency with which mycotic aneurysms, etc., may follow.

The authors are, I think, a little too absolute in their unfavorable prognosis. There are undoubted recoveries, rare though they be.

Under the heading of "clinical forms" they consider those instances in which the disturbances of the patient's general condition is in the foreground; those in which the painful phenomena—arthritis, myalgic, etc.—are the most prominent features; those in which the visceral changes are notabe, embolism, degenerative changes giving rise to Hippocratic fingers, nervous forms of the disease, renal forms, respiratory or more rarely, the occasional cardioplegic forms. They mention the occasional termination with an acute exacerbation of the symptoms dependent upon renal or cardiac insufficiency or upon an aggravation of the septicemia or a secondary infection. Finally they acknowledge that in some cases the valvular lesions may be primary, arising on curtains previously unaffected. They insist that the foci are frequently parietal making the diagnosis difficult. In the experience of the reviewer parietal endocarditis though common is rarely unassociated with valvular lesion.

On pages 55 and 57 there is an excellent summary of the differential diagnostic features. The authors are perhaps a trifle too dogmatic in asserting that emboli are not seen in rheumatic cardiac disease. There are, of course, instances of embolism in subacute rheumatic heart disease with thrombosis of the auricular appendages in auricular fibrilla-

tion, and the reviewer has seen repeated embolisms due to massive thrombosis on the wall of the left auricle in an instance which simulated subacute infective endocarditis to an extraordinary degree.

They justly point out that in doubtful cases, in childhood and adolescence, one should turn toward the diagnosis of rheumatic endocarditis. The reviewer is, however, inclined to believe that secondary bacterial endocarditides are commoner in childhood than is generally believed. In only 6 of 146 instances of streptococcal endocarditis of subacute or prolonged course in his series were the subjects in the first decade of life, yet the proportion of children to adults in his material was for a long time very low. Again one must remember that the cultivation of streptococci from the blood of patients with rheumatic fever is not rare, and of itself does not justify a diagnosis of vegetative or ulcerative endocarditis.

The writers wisely refer to the frequent slow growth of the nonhemolytic streptococci and advise the observation of the cultures for eight days or more. The reviewer would extend this even further. He has seen abundant growth appearing first thirteen days after the making of the cultures.

In their discussion of the *treatment of rheumatic endocarditis* the writers are sanguine as to the *preventive* value of salicylates. They devote a page and a half to the discussion of the intravenous use of salicylate of sodium in rheumatic carditis. They recognize its dangers —the sclerosing action on the veins, "salicylate shock," and, in one instance, sudden death, but they feel that with care, this method of treatment is free from danger and is sometimes of value. They advise 10 per cent solutions of salicylate of sodium in 10 per cent glucose. At first the dose should not be above 0.5 sodium salicylate. This dose should be increased gradually never to more than 1.5-2 per dose. Salicylate of sodium, 2 grams twice daily, is sufficient usually to keep the organism under the influence of the drug.

There are many and the writer is one, who feel that the intravenous use of salicylate of sodium is hardly justifiable at the present time. He is unconvinced that the advantages outweigh the dangers. He may be overcautious, but intravenous treatment seems to him justifiable only when the result obtained is more or less specific and when it can be obtained by no other method. Much of the modern intravenous treatment seems to him unnecessary, meddlesome and even dangerous, besides being annoying, inconvenient and expensive to the patient.

The treatment of *septic infective endocarditis* is then reviewed. The authors are conservative as to the value of most of the methods of specific or nonspecific treatment. The treatment by cacodylate of sodium advised by Capps is wrongly described as intravenous instead of subcutaneous. With regard to *subacute malignant endocarditis* or that of

*long duration* the authors conclude that "the malady remains, in the present state of our knowledge, beyond the resources of therapy."

On the whole this volume is a remarkably clear, wise and vivid discussion of endocarditis. It is distinctly a clinical description with little discussion of the anatomical changes. As such there are few, if any, better articles on the subject in modern literature.

*W. S. T.*

NOUVEAU TRAITÉ DE PATHOLOGIE INTERNE. MALADIES DU COEUR ET DES VAISSEAUX. By Charles Laubry with the collaboration of Daniel Routier, J. Walser and Ed. Doumier. Paris, 1930 (one or two volumes), Doin & Cie.

This work (1,200 pages with 242 illustrations and 10 large color plates) is more than a pathological study; it is an attempt to classify diseases of the heart and blood vessels, to discuss etiology, symptoms, signs, functional disturbances, gross and microscopic pathology, treatment and prognosis. It is founded on the authors' own work and study; is carefully written, systematically arranged and well illustrated. At times one feels that the systematization is carried to the point where it becomes confusing rather than helpful, that a familiar subject (such as the arrhythmias) is being rewritten or that an important one (as thrombo-angiitis obliterans) is passed over rather lightly, but these are minor criticisms. The section on diseases of the blood vessels is particularly interesting, and throughout the book the beautiful illustrations, the emphasis on pathological findings and the fundamental good sense of the suggestions for treatment (even if one does not share the authors' faith in the value of iodides) make this a valuable book.

*E. H.*

HYPERTENSION. By Leslie T. Gager, M.D., Clinical Professor of Medicine at the George Washington University; Attending Physician Gallinger Municipal Hospital; Associate Physician George Washington University Hospital. Baltimore, 1930, 158 pages, Williams & Wilkins Co.

In this monograph a splendid exposition of the story of blood pressure from its inception to the present time has been accomplished. The book is very well written and thoughtfully conceived, so that it is a pleasure to read it and follow the writer's impression derived from the vast literature on this subject and from his practical experience. It is a great delight, for some of us at least, to find a clinician who is willing to acknowledge that functional pathology is of equal importance in the practice of the art of medicine with pathological anatomy, and that some conditions, e.g., hypertension, are diseases attributable to patho-

physiology and not to deviations from the normal that may be demonstrated to the eye or touch. In the development of his subject Gager has a singularly happy faculty in picking out the historical stepping stones that are both interesting and significant, so that this part of the work becomes a source of instruction instead of a dry category of dates and happenings as is so often the case. The review of the facts in regard to hypertension are exceedingly well culled out, and the arguments pro and con on any doubtful point are fairly given. The generous statement that (p. 107) "As a matter of fact, it has been my experience that significant and lasting reduction in severe chronic hypertension is frequently impossible either by drugs, venesection or withdrawal of cerebro-spinal fluid," is refreshing in its sincerity and honesty; it corresponds to the experiences which all physicians have gone through and is vastly different from the impression created by many reports which advocate certain forms of treatment as being almost infallible. Gager has used potassium thiocyanate with satisfactory results in patients with uncomplicated genuine or essential hypertension; he has been largely responsible for the favorable reception this drug is receiving in this country. This volume on hypertension may be recommended to the physician who desires a review of this subject that embodies a thoughtful presentation, logical conclusions and a sparkling literary form that is rare in a medical book.

*H. O. M.*

RECENT ADVANCES IN CARDIOLOGY. By C. F. T. East and C. W. C. Bain. Philadelphia, 1929, P. Blakiston's Son & Co.

It is difficult indeed to restrain one's enthusiasm in writing of this small book. It is small only in comparison with the average textbook upon diseases of the heart, for it contains nearly three hundred and fifty pages, and is surprisingly complete. The authors have "tried to give a summary of the new knowledge, and also to describe its bearing upon problems which are not primarily cardiac." In a review so brief as this it is impossible to indicate how well they have succeeded, but of their success there can be no reasonable doubt. Not only have they given admirable summaries of recent advances in our knowledge of circulatory diseases, but they have also supplied that additional thing for lack of which so many attempts of this kind have failed, namely, a running critical commentary that is well-founded, authoritative, and refreshingly sane. The presentation is concise, as it must and should be, but ample space is devoted to every important phase of each subject; for example, such matters as the circus movement of auricular flutter and fibrillation are discussed in detail and with admirable clarity. The volume is not restricted to matters of diagnosis; general treatment and digitalis therapy are each given an entire long chapter.

From a series of chapters so uniformly excellent it would be gratuitous to select any one for particular praise, but one can scarcely neglect to mention the discussion of circulatory failure as distinguished from cardiac failure. Altogether, the volume is one to be commended without hesitation to all who wish to bring their knowledge of cardiology up to date. It is superior in almost every respect to many of the textbooks now available.

*H. M. M.*

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